

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: 12 GITOMEN Examiner #: 69634 Date: 3/11/02
 Art Unit: 1623 Phone Number 30 8-0732 Serial Number: 09/918,234
 Mail Box and Bldg/Room Location: 8B19 Results Format Preferred (circle): PAPER DISK E-MAIL
7A11

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

JAN

Jan Delaval
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Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: <u>3/18/02</u>	Bibliographic <input checked="" type="checkbox"/>	Dr.Link _____
Date Completed: <u>3/18/02</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: <u>30</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>+90</u>	Other _____	Other (specify) _____

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FILE 'REGISTRY' ENTERED AT 15:26:42 ON 18 MAR 2002
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STRUCTURE FILE UPDATES: 17 MAR 2002 HIGHEST RN 401569-84-4
DICTIONARY FILE UPDATES: 17 MAR 2002 HIGHEST RN 401569-84-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNnote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAPLUS files between
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during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved. Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAPLUS files
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CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
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receive a credit for any duplicate searches.

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L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 9012-42-4 REGISTRY
CN Cyclase, adenylate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Adenyl cyclase
CN Adenylate cyclase
CN Adenylyl cyclase
CN E.C. 4.6.1.1
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHM, EMBASE,
IFICDB, IFIPAT, IFIUDB, IPA, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

18645 REFERENCES IN FILE CA (1967 TO DATE)

42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

18651 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:182399

REFERENCE 2: 136:181653

REFERENCE 3: 136:179700

REFERENCE 4: 136:179596

REFERENCE 5: 136:178618

REFERENCE 6: 136:178328
REFERENCE 7: 136:178306
REFERENCE 8: 136:178256
REFERENCE 9: 136:178255
REFERENCE 10: 136:178252

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 15:26:54 ON 18 MAR 2002

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FILE COVERS 1907 - 18 Mar 2002 VOL 136 ISS 12
FILE LAST UPDATED: 17 Mar 2002 (20020317/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d all tot 176

L76 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:107680 HCAPLUS

DN 136:145271

TI Marker for antidepressant therapy and methods related thereto

IN **Rasenick, Mark M.; Donati, Robert J.; Toki, Sadamu**

PA The Board of Trustess of the University of Illinois, USA

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-566

CC 1-11 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2002010763	A2	20020207	WO 2001-US23851	20010730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-221874P P 20000729

AB The present invention relates generally to methods for detg. the effectiveness of ongoing **antidepressant** therapy via anal. of the assocd. of **Gs.alpha.** with components of the **plasma membrane** or **cytoskeleton** of **cells** from **peripheral** tissues of the **depressed** individual as well as to methods involved in screening for effective **antidepressant** agents via their ability to cause a difference in the assocn. of **Gs.alpha.** with components of the **plasma membrane** or **cytoskeleton** of **cells**.

ST **GSalpha** **adenylyl cyclase** marker
antidepressant therapy

IT **G proteins (guanine nucleotide-binding proteins)**
 RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)

(**Gs (adenylate cyclase-stimulating)**; **plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT Nerve
 (neuron; **plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **Antidepressants**
Drug screening
Erythrocyte
Leukocyte
 Neuroglia
Platelet (blood)
 (plasma membrane and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **Fibroblast**
 (skin; **plasma membrane** and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT **9012-42-4**
 RL: ANT (Analyte); ANST (Analytical study)
 (plasma membrane and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 50-53-3, Chlorpromazine, biological studies 5560-72-5, Iprindole 54910-89-3, Fluoxetine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (plasma membrane and **cytoskeleton cell Gs.alpha.** and **type VI adenylyl cyclase** as markers for studying the efficacy of **antidepressant** therapy)

AN 2001:402217 HCAPLUS
 DN 135:205470
 TI Chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**
 AU **Donati, Robert J.**; Thukral, Chandrashekhar; **Rasenick, Mark M.**
 CS Departments of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, Chicago, IL, USA
 SO Molecular Pharmacology (2001), 59(6), 1426-1432
 CODEN: MOPMA3; ISSN: 0026-895X
 PB American Society for Pharmacology and Experimental Therapeutics
 DT Journal
 LA English
 CC 1-11 (Pharmacology)
 AB Previous studies have demonstrated that chronic treatment of C6 glioma **cells** with the **antidepressants** desipramine and fluoxetine increases the Triton X-100 soly. of the **G protein Gs.alpha.**.. The **antidepressants** also caused a 50% decrease in the amt. of **Gs.alpha.** localized to caveolae-enriched **membrane** domains. In this study, laser scanning confocal microscopy reveals that **Gs.alpha.** is localized to the **plasma membrane** as well as the cytosol in both treated and control **cells**. However, striking differences are seen in the distribution of **Gs.alpha.** in the long cellular processes after chronic treatment with these **antidepressant** drugs. Control **cells** display **Gs.alpha.** along the entire process with an esp. high concn. of that **G protein** at the distal ends. Desipramine- or fluoxetine-treated **cells** show a more centralized clustering of **Gs.alpha.** in the Golgi region of the **cell** and a drastic redn. of **Gs.alpha.** in the cellular processes. There is no change in the distribution of **Go.alpha.** after desipramine treatment and the antipsychotic drug chlorpromazine does not alter **Gs.alpha.**.. These results suggest that **antidepressant**-induced changes in the assocn. of **Gs.alpha.** with the **plasma membrane** may translate into altered cellular localization of this signal transducing **protein**. Thus, modification of the coupling between **Gs**-coupled receptors and **adenyllyl cyclase** may underlie both **antidepressant** therapy and **depressive** illnesses. This report also suggests that modification of the **membrane** domain occupied by **Gs.alpha.** might represent a mechanism for chronic **antidepressant** effects.

ST **antidepressant G protein Gsalpha**
 membrane signaling

IT **G proteins (guanine nucleotide-binding proteins)**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (**Gs (adenylate cyclase-stimulating), .alpha.**; chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**)

IT **Antidepressants**
 Cell membrane
 Cytoskeleton
 Signal transduction, biological
 (chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**)

IT Cytoplasm
 (cytosol; chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs.alpha.**)

IT 50-47-5, Desipramine 50-53-3, Chlorpromazine, biological studies

54910-89-3, Fluoxetine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chronic treatment of C6 glioma **cells** with **antidepressant** drugs results in a redistribution of **Gs** **.alpha.**)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Bayewitch, M; Mol Pharmacol 2000, V57, P820 HCAPLUS
- (2) Brown, D; J Biol Chem 2000, V275, P17221 HCAPLUS
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L76 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:659522 HCAPLUS

DN **131:281588**

TI Diagnosis and treatment of neuropsychiatric disorders based on the
pituitary **adenylate cyclase**-activating peptide gene
PACAP

IN Chen, Hong; Freimer, Nelson B.

PA Millennium Pharmaceuticals, Inc., USA; The Regents of the University of
California

SO PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12P019-34

ICS C12Q001-68; G01N033-53
 CC 1-11 (Pharmacology)
 Section cross-reference(s): 3, 13
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9951762	A1	19991014	WO 1999-US7401	19990402
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9934696	A1	19991025	AU 1999-34696	19990402
	EP 1068347	A1	20010117	EP 1999-916355	19990402
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
PRAI	US 1998-80570P	P	19980403		
	WO 1999-US7401	W	19990402		
AB	The present invention relates to the mammalian PACAP gene and the discovery that the PACAP gene is linked to the short arm of chromosome 18 in a region of the chromosome involved in mediating neuropsychiatric disorders such as bipolar-affective disorder. The invention relates to methods for the identification of compds. that modulates the expression of PACAP and to using such compds. as therapeutic agents in the treatment of PACAP disorders. The invention also relates to methods for the diagnostic evaluation, genetic testing and prognosis of PACAP-mediated disorders, and to methods and compns. for the treatment of these disorders. The invention also relates to use of the PACAP gene and/or gene products as markers for fine structure mapping of a region of human chromosome 18, including a region of the chromosome involved in mediating neuropsychiatric disorders.				
ST	pituitary adenylate cyclase activating peptide gene neuropsychiatric disorder; PACAP gene mapping neuropsychiatric disorder diagnosis treatment				
IT	Gene, animal RL: ANT (Analyte); BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (PACAP; diagnosis and treatment of neuropsychiatric disorders based on the pituitary adenylate cyclase -activating peptide gene PACAP)				
IT	Mutation (deletion, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary adenylate cyclase -activating peptide gene PACAP)				
IT	Drug screening Genetic mapping Mental disorder Nucleic acid amplification (method) Nucleic acid hybridization Psychotropics Schizophrenia Susceptibility (genetic) (diagnosis and treatment of neuropsychiatric disorders based on the pituitary adenylate cyclase -activating peptide gene PACAP)				
IT	cDNA sequences (for human pituitary adenylate cyclase -activating peptide)				
IT	Diagnosis (genetic; diagnosis and treatment of neuropsychiatric disorders based on the pituitary adenylate cyclase -activating				

- peptide gene PACAP)
- IT Chromosome
(human 18; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT Mutation
(insertion, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT **Mental disorder**
(**mania**; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT **Mental disorder**
(**manic bipolar disorder**; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT DNA sequences
(of human gene PACAP encoding pituitary **adenylate cyclase**-activating peptide)
- IT Protein sequences
(of human pituitary **adenylate cyclase**-activating peptide)
- IT Mutation
(substitution, diagnosis by detection of; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT **134688-73-6 245755-73-1**
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT **137061-48-4**, Pituitary **adenylate cyclase**-activating peptide
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT 9075-08-5, Restriction endonuclease
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- IT **246038-54-0**
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; diagnosis and treatment of neuropsychiatric disorders based on the pituitary **adenylate cyclase**-activating peptide gene PACAP)
- RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
- (1) Ohkubo; DNA and Cell Biology 1992, V11(1), P21 HCAPLUS
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L76 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:547159 HCAPLUS

DN 131:270413

TI **G protein**-coupled cyclic AMP signaling in postmortem brain of subjects with mood disorders: effects of diagnosis, suicide, and treatment at the time of death

AU Dowlatsahi, Dar; MacQueen, Glenda M.; Wang, Jun-Feng; Reiaich, James S.;

Young, L. Trevor
 CS Mood Disorders Program, McMaster University, Hamilton, ON, L8N 3ZS, Can.
 SO J. Neurochem. (1999), 73(3), 1121-1126
 CODEN: JONRA9; ISSN: 0022-3042
 PB Lippincott Williams & Wilkins
 DT Journal
 LA English
 CC 14-10 (Mammalian Pathological Biochemistry)
 AB Components of cAMP signaling were examd. in postmortem cerebral cortex of a well characterized group of patients with mood disorders and nonpsychiatric control subjects. We measured **G protein** levels, **adenyllyl cyclase** (AC) activity, and CREB levels in cerebral cortex of the subjects with respect to diagnosis, treatment, and suicide. There was no effect of diagnosis on any measure, except for a trend toward decreased **stimulated** AC activity in subjects with mood disorders relative to control subjects. We also detected a significant effect of suicide on temporal cortex CREB levels in subjects that died as a result of suicide relative to those that did not, which was more evident in patients with major **depressive** disorder. Bipolar disorder (BD) subjects treated with anticonvulsants at the time of death had decreased temporal cortex CREB levels relative to those not receiving anticonvulsants. Furthermore, we found a trend toward decreased occipital cortex **G.alpha.s** (short) levels in BD subjects treated with lithium. These results support the hypothesis of altered cAMP signaling in mood disorders and raise the possibility that factors other than diagnosis, such as treatment and suicide, may be relevant to **cell**-signaling abnormalities reported in the literature.
 ST suicide **depression** brain cAMP signaling
 IT Transcription factors
 RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
 (CREB (cAMP-responsive element-binding); **G protein** -coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT Second messenger system
 (**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT **G proteins (guanine nucleotide-binding proteins)**
 RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
 (**Gs (adenylate cyclase-stimulating)**, **.alpha.** subunit; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT Brain
 (cerebral cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT **Mental disorder**
 (**depression**, major; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT Anticonvulsants
 (effect on temporal cortex CREB levels in humans with bipolar disorder)
 IT **Mental disorder**
 (**manic bipolar disorder**; CREB levels in temporal cortex of humans with)
 IT **Mental disorder**
 (mood-affecting; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)
 IT Brain

(occipital cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Death
(suicide; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT Brain
(temporal cortex; **G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT **9012-42-4, Adenylyl cyclase**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

IT 60-92-4, CAMP
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**G protein**-coupled cAMP signaling in postmortem brain of humans with mood disorders and effects of diagnosis, suicide, and treatment at time of death)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L76 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:547158 HCAPLUS

DN 131:281415

TI Treatment of C6 glioma **cells** and rats with **antidepressant** drugs increases the detergent extraction of **Gs.alpha.** from **plasma membrane**

AU **Toki, Sadamu; Donati, Robert J.; Rasenick, Mark M.**

CS Departments of Physiology and Biophysics, University of Illinois College of Medicine, Chicago, IL, 60612-7342, USA

SO J. Neurochem. (1999), 73(3), 1114-1120
CODEN: JONRA9; ISSN: 0022-3042

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1-11 (Pharmacology)

AB Results from previous studies suggested that chronic treatment of rats or C6 glioma **cells** with **antidepressants** augments the coupling between **Gs** and **adenylyl cyclase**. As these effects on C6 glioma **cells** are seen in the absence of presynaptic input, several **antidepressant** drugs may have a direct "postsynaptic" effect on their target **cells**. It was hypothesized that the target of **antidepressant** action was some **membrane protein** that may regulate coupling between **G proteins** and **adenylyl cyclase**. To test this, C6 glioma **cells** were treated with amitriptyline, desipramine, iprindole, or fluoxetine for 3 days. Chlorpromazine served as a control for these treatments. **Membrane proteins** were extd. sequentially with Triton X-100 and Triton X-114 from C6 glioma **cells**. Triton X-100 extd. more **Gs.alpha.** in **membranes** prep'd. from **antidepressant**-treated C6 glioma **cells** than from control groups. In addn., **cell** fractionation studies revealed that the amt. of **Gs.alpha.** in caveolin-enriched domains was reduced after **antidepressant** treatment and that **adenylyl cyclase** comigrated with **Gs.alpha.** in the gradients. These data suggest that some postsynaptic component that increases availability of **Gs** to activate effector mols., such as **adenylyl cyclase**, might be a target of **antidepressant** treatment.

ST **antidepressant G protein adenylyl cyclase** signaling

IT **G proteins (guanine nucleotide-binding proteins)**
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (adenylyl cyclase-regulating;
 antidepressant drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)

IT **Antidepressants**
 Signal transduction, biological
 (antidepressant drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)

IT **Proteins, specific or class**
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (membrane; antidepressant drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole 54910-89-3, Fluoxetine
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antidepressant drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)

IT **9012-42-4, Adenylyl cyclase**
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (antidepressant drug mechanism of action: **Gs.alpha.-adenylyl cyclase** signaling mediation)

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L76 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:150163 HCAPLUS

DN 131:13783

TI Alterations of tubulin function caused by chronic **antidepressant** treatment in rat brain

AU Kamada, Hiroki; Saito, Toshikazu; Hatta, Shinichi; **Toki, Sadamu**;
Ozawa, Hiroki; Watanabe, Masayuki; Takahata, Naohiko

CS Department of Neuropsychiatry, School of Medicine, Sapporo Medical
University, Sapporo, 060-8556, Japan

SO Cell. Mol. Neurobiol. (1999), 19(1), 109-117
CODEN: CMNEDI; ISSN: 0272-4340

PB Kluwer Academic/Plenum Publishers

DT Journal

LA English

CC 1-11 (Pharmacology)

AB **Antidepressants** have been used clin. for many years; however, the neurochem. mechanism for their therapeutic effect has not been clarified yet. Recent reports indicate that chronic **antidepressant** treatment directly affects the postsynaptic membrane to increase the coupling between the **stimulatory** GTP-binding (G) **protein, Gs**, and **adenylyl cyclase**. Tubulin, a **cytoskeletal** element, is involved in the **stimulatory** and inhibitory regulation of **adenylyl cyclase** in rat cerebral cortex via direct transfer of GTP to **G proteins**. In this study, the authors investigated whether the functional change of the **adenylyl cyclase** system caused by chronic **antidepressant** treatment involves an alteration of tubulin function in the regulation of **adenylyl cyclase** activity. Male Sprague-Dawley rats were treated once daily with amitriptyline or saline by i.p. injection (10 mg/kg) for 21 days, and their cerebral cortex membranes and GppNHp-liganded tubulin (tubulin-GppNHp) were prepd. for what. GppNHp-**stimulated adenylyl cyclase** activity in cortex membranes from amitriptyline-treated rats was significantly higher than that in control membranes. Furthermore, tubulin-GppNHp prepd. from amitriptyline-treated rats was more potent than that from control rats in the **stimulation of adenylyl cyclase** activity in the cortex membranes of the controls. However, there was no significant difference in **manganese-stimulated adenylyl cyclase** activity between control and amitriptyline-treated rats. The present results suggest that chronic **antidepressant** treatment enhances not only the coupling between **Gs** and the catalytic subunit of **adenylyl cyclase** but also tubulin interaction with **Gs** in the cerebral cortex of the rat.

ST tubulin function alteration **antidepressant** brain

- IT Proteins, specific or class
 RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study);
 PROC (Process)
 (GTP-binding; alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT **Antidepressants**
 (alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT Tubulins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT **G proteins (guanine nucleotide-binding proteins)**
 RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study);
 PROC (Process)
 (alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT Brain
 (cerebral cortex; alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT 50-48-6, Amitriptyline
 RL: BAC (Biological activity or effector, except adverse); BIOL
 (Biological study)
 (alterations of tubulin function caused by chronic
antidepressant treatment in brain)
- IT **9012-42-4, Adenylyl cyclase**
 RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
 BIOL (Biological study)
 (alterations of tubulin function caused by chronic
antidepressant treatment in brain)

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L76 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:31135 HCAPLUS

DN 126:69607

TI **G protein**-mediated signal transduction as a target of
antidepressant and antibipolar drug action: evidence from model

systems

AU **Rasenick, Mark M.**; Chaney, Kimberly A.; Chen, Jiang
 CS College Medicine, University Illinois, Chicago, IL, 60612-7342, USA
 SO J. Clin. Psychiatry (1996), 57(Suppl. 13), 49-58
 CODEN: JCLPDE; ISSN: 0160-6689
 PB Physicians Postgraduate Press
 DT Journal; General Review
 LA English
 CC 1-0 (Pharmacology)
 AB A **review**, with 38 refs., discussing evidence that altered **G protein**-mediated signal transduction provides at least one piece with which to complete the mosaic defining the cascade of mol. events resulting in **antidepressant** or antimanic action. It is demonstrated that simple, exptl. accessible systems represent ideal models with which to det. the nature of candidate **antidepressant** or antimanic compds.

ST **review G protein antidepressant**
 mania therapy; signal transduction **antidepressant** mania therapy
review; bipolar disease therapy **G protein**
review

IT **Antidepressants**
Bipolar disorder
Mania
 Signal transduction (biological)
 (G protein-mediated signal transduction as a target of **antidepressant** and antibipolar drug action)

IT **G proteins (guanine nucleotide-binding proteins)**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (signal transduction mediated by **G proteins** as a target of **antidepressant** and antibipolar drug action)

IT Biological simulation
 (signal transduction mediated by **G proteins** as a target of **antidepressant** and antibipolar drug action as studied by)

L76 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
 AN 1995:886523 HCAPLUS
 DN 123:306475
 TI Chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content

AU Chen, Jiang; **Rasenick, Mark M.**
 CS Dep. Physiology Biophys., Univ. Illinois Coll. Med., Chicago, USA
 SO J. Pharmacol. Exp. Ther. (1995), 275(1), 509-17
 CODEN: JPETAB; ISSN: 0022-3565
 DT Journal
 LA English
 CC 1-11 (Pharmacology)
 AB It has been suggested that the mol. basis of **antidepressant** action involves postreceptor components. Results from the studies have suggested that a **G protein** (**Gs**) is one of those targets and that chronic **antidepressant** treatment facilitates the activation of **adenylyl cyclase** by **Gs.alpha.** This report represents an attempt to define which aspects of **G protein** function are altered by chronic **antidepressant** treatment. Rats were treated for 21 days with amitriptyline, desipramine, ABT 200 (a pyrrolidine with putative **antidepressant** effects) or electroconvulsive shock, and membranes were prep'd. from the cerebral cortexes. Each of these treatments caused an increase in membrane **adenylyl cyclase** assayed in the presence of guanylyl-5'-imidodiphosphate (.gtoreq. 1 .mu.M). Results of acute **antidepressant** treatments were no different than those of control treatment. Chronic treatment with amphetamine, which inhibits neurotransmitter reuptake without displaying **antidepressant** effect, was also ineffective in increasing **Gs.alpha.**
stimulation of adenylyl cyclase. Chronic

antidepressant treatment did not change the content of **G protein**, as no change at the level of **Gs.alpha.**, **Gi.alpha.**, **Go.alpha.** or **G.beta.** **protein** was detected by immunoblotting. Although there was no change in the amt. of **G proteins**, **antidepressant** treatment increased the no. of active **Gs.alpha./adenylyl cyclase** complexes immunopptd. by an anti-**Gs.alpha.** antibody. It is suggested that chronic **antidepressant** treatment alters certain membrane components such that a greater proportion of **Gs.alpha.** is activated, **Gs.alpha.** enjoys a more fruitful interaction with **adenylyl cyclase**, or both.

ST **antidepressant G protein adenylyl cyclase brain**

IT **Antidepressants**

Cell membrane

(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **G proteins (guanine nucleotide-binding proteins)**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **Brain**

(cerebral cortex, chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **Convulsion**

(electro-, chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline 148152-63-0, ABT 200

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

IT **9012-42-4, Adenylyl cyclase**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic **antidepressant** treatment facilitates **G protein** activation of **adenylyl cyclase** without altering **G protein** content)

L76 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:318539 HCAPLUS

DN 122:96306

TI Chronic treatment of C6 glioma **cells** with **antidepressant** drugs increases functional coupling between a **G protein** (**Gs**) and **adenylyl cyclase**

AU Chen, Jiang; Rasenick, Mark M.

CS Dep. Physiol., Univ. Illinois Coll. Med., Chicago, IL, USA

SO J. Neurochem. (1995), 64(2), 724-32

CODEN: JONRA9; ISSN: 0022-3042

DT Journal

LA English

CC 1-11 (Pharmacology)

AB It has been reported that **antidepressant** treatment in rats results in a significant increase of **Gs**-mediated **stimulation of adenylyl cyclase** and this effect correlates well with the clin. therapeutic response. This increased activity occurs despite a down-regulation of several receptors linked normally to the **stimulation** of that enzyme. To distinguish between these effects and to det. whether presynaptic components of the **cell** are required, C6 glioma **cells**

were treated with **antidepressants**. Tricyclic (amitriptyline and desipramine) or atypical (iprindole) **antidepressant** exposure to C6 cells for 5 days significantly increased guanylyl-5'-imidodiphosphate [Gpp(NH)p]-**stimulated adenylyl cyclase** activity in **membrane** preps. in a manner similar to that seen for rat brain **membranes** after 21-day treatment. This effect was drug dose and exposure time dependent. Nevertheless, **stimulation of adenylyl cyclase** by isoproterenol was decreased after **antidepressant** treatment. By comparison, the **antidepressant**-induced .beta.-receptor desensitization occurred earlier than the enhancement of Gpp(NH)p-activated **adenylyl cyclase**, and extensive desensitization of .beta. receptors by isoproterenol treatment did not enhance the Gpp(NH)p-**stimulated adenylyl cyclase** activity. These results indicated that the **antidepressants** have a direct effect on cell signaling and this enhanced Gpp(NH)p-**stimulated adenylyl cyclase** activity is not correlated with desensitization of .beta.-adrenergic receptor **stimulated adenylyl cyclase**. These data contribute to the suggestion that G proteins (esp. Gs) are the target of **antidepressant** actions. Immunoblotting showed that neither the no. of G protein subunits (.alpha.s, .alpha.i, .alpha.0, and .beta.) nor their assocn. with the **plasma membrane** was changed after **antidepressant** treatment. Thus, these results are consistent with the hypothesis that chronic **antidepressant** treatment acts directly at the postsynaptic **membrane** to increase the coupling between Gs and **adenylyl cyclase**.

- ST **antidepressant G protein adenylyl cyclase** coupling; glioma **antidepressant G protein adenylyl cyclase**
- IT **Antidepressants**
(chronic treatment of C6 glioma cells with **antidepressant** drugs increases functional coupling between G protein (Gs) and **adenylyl cyclase**)
- IT **G proteins (guanine nucleotide-binding proteins)**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(Gs (adenylate cyclase-stimulating), chronic treatment of C6 glioma cells with **antidepressant** drugs increases functional coupling between G protein (Gs) and **adenylyl cyclase**)
- IT **Neuroglia**
(neoplasm, chronic treatment of C6 glioma cells with **antidepressant** drugs increases functional coupling between G protein (Gs) and **adenylyl cyclase**)
- IT **Receptors**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.beta.-adrenergic, chronic treatment of C6 glioma cells with **antidepressant** drugs increases **adenylyl cyclase** activity in relation to desensitization of .beta.-adrenergic receptors)
- IT 34273-04-6, Guanylyl-5'-imidodiphosphate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(chronic treatment of C6 glioma cells with **antidepressant** drugs increases Gpp(NH)p-**stimulated adenylyl cyclase**)
- IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic treatment of C6 glioma cells with **antidepressant** drugs increases functional coupling between

G protein (Gs) and adenylyl cyclase)

L76 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
 AN 1993:667983 HCAPLUS
 DN 119:267983
 TI Cerebral cortex **Gs.alpha. protein** levels and forskolin-**stimulated** cyclic AMP formation are increased in bipolar affective disorder
 AU Young, L. Trevor; Li, Peter P.; Kish, Stephen J.; Siu, Kin Po; Kamble, Arvind; Hornykiewicz, Oleh; Warsh, Jerry J.
 CS Sect. Biochem. Psychiatry, Clarke Inst. Psychiatry, Toronto, ON, M5T 1R8, Can.
 SO J. Neurochem. (1993), 61(3), 890-8
 CODEN: JONRA9; ISSN: 0022-3042
 DT Journal
 LA English
 CC 14-10 (Mammalian Pathological Biochemistry)
 AB Exptl. animal and **peripheral blood cell** studies point to guanine nucleotide regulatory (**G**) **protein** disturbances in bipolar affective disorder. The authors have previously reported elevated prefrontal cortex **Gs.alpha. protein** in bipolar affective disorder and have now extended these preliminary observations in a larger no. of subjects, assessing the brain regional specificity of these changes in greater detail, detg. the functional biochem. correlates of such changes, and evaluating their diagnostic specificity. **Membrane G protein (Gs.alpha., Gi.alpha., Go.alpha., and G.beta.)** immunoreactivities were estd. by western blotting in postmortem brain regions obtained from 10 patients with a DSMIII-R diagnosis of bipolar affect disorder and 10 nonpsychiatric controls matched on the basis of age, postmortem brain regions obtained from 10 patients with a DSMIII-R diagnosis of bipolar affective disorder and 10 nonpsychiatric controls matched on the basis of age, postmortem delay, and brain pH. To examine whether there were functional correlates to the obsd. elevated **Gs.alpha.** levels, basal and GTP.gamma.S- and forskolin-**stimulated** cAMP prodn. was detd. in the same brain regions. Compared with controls, **Gs.alpha.** (52-kDa species) immunoreactivity was significantly ($p < 0.05$) elevated in prefrontal (+36%), temporal (+65%), and occipital (+96%) cortex but not in hippocampus (+28%), thalamus (-23%), or cerebellum (+21%). In contrast, no significant differences were found in the other **G protein** subunits (**Gi.alpha., Go.alpha., G.beta.**) measured in these regions. Forskolin-**stimulated** cAMP prodn. was significantly increased in temporal (+31%) and occipital (+96%) cortex but not in other regions. No significant differences were apparent in basal or GTP.gamma.S-**stimulated** cAMP prodn. A significant correlation was obsd. between forskolin-**stimulated** cAMP formation and **Gs.alpha.** (52 kDa) immunoreactivity when examd. across these cortical regions. The obsd. increase in **Gs.alpha.** may be specific to bipolar disorders as no significant differences were detected in **Gs.alpha.** levels in temporal cortex from patients with either schizophrenia or Alzheimer's disease. In summary, the present study confirms and extends the authors' earlier findings and supports the notion that increased **Gs.alpha.** levels and possibly **Gs.alpha.-adenylyl cyclase-mediated** signal transduction are relevant to the pathophysiol. of bipolar affective disorder.
 ST affective disorder brain **Gs protein**
 IT Signal transduction, biological
 (**G protein-mediated**, in brain regions, in bipolar affective disorder of humans)
 IT Brain, composition
 (**Gs.alpha. protein** levels and cAMP formation in regions of, in bipolar affective disorders of humans)

- IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(G.beta., of brain regions, in bipolar affective disorders of humans)
- IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(Gi (adenylate cyclase-inhibiting), .alpha.-subunit, of brain regions, in bipolar affective disorders of humans)
- IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(Go, .alpha.-subunit, of brain regions, in bipolar affective disorders of humans)
- IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(Gs (adenylate cyclase-stimulating), .alpha.-subunit, of brain regions, in bipolar affective disorders of humans)
- IT **Mental disorder**
(manic depression, Gs.alpha. proteins and cAMP formation increase in brain regions in, in humans)
- IT 60-92-4, CAMP
RL: FORM (Formation, nonpreparative)
(formation of, increase in, in brain regions of humans with bipolar affective disorder)
- L76 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:512079 HCAPLUS
DN 115:112079
TI The effects of electroconvulsive shock on receptor-G
protein-adenylate cyclase coupling
AU Ozawa, Hiroki; **Rasenick, Mark M.**; Takahata, Naohiko; Saito, Toshikazu
CS Dep. Neuropsychiatry, Sapporo Med. Coll., Sapporo, Japan
SO Jpn. J. Psychiatry Neurol. (1991), 45(1), 137-8
CODEN: JJPNEA; ISSN: 0912-2036
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB In rats, the long-term administration of electroconvulsive shock (ECS) induced a significant decrease in the no. of brain beta-adrenergic receptors without altering the affinity of the sites. In contrast to the above results, Gpp(NH)p, NaF or forskolin **stimulated** **adenylate cyclase** (AC) activity was increased in the rat cerebral cortex membranes. These effects by ECS were progressive in a time-dependent manner, but no significant differences were seen in sham or acute treatment. The percent inhibition induced by GppNHp as well as the IC50 for that compd. was equiv. in all the groups and the chem. elimination of GTP-binding **proteins (G protein**
) abolished the enhancement of AC by the chronic ECS treatment. The disocn. const. (Kd) and maximal binding (Bmax) for AAGTP (a hydrolysis-resistant, photoaffinity GTP analog) to synaptic membrane **G proteins** was unchanged after the ECS treatment. Thus, it is unlikely that there was any change in the quantity or GTP-binding capacity of **G proteins**. However, the transfer of [32P]-AAGTP from Gi/o to Gs was accelerated by the chronic ECS treatment. Treatment alters some aspect of the milieu in which **G proteins** interface with their receptors, effectors and with one another, esp. under a "G protein" upon the system. Such neurochem. changes in ECS appear to be similar to those of **antidepressant** drug therapy.
- ST electroconvulsive shock receptor **protein adenyate cyclase**; adrenergic beta receptor coupling electroconvulsive shock; **G protein** receptor coupling electroconvulsive shock; **adenylate cyclase** receptor coupling electroconvulsive shock

- IT **Proteins, specific or class**
 RL: BIOL (Biological study)
 (adenylate cyclase-regulating, guanine nucleotide-binding, G, .beta.-adrenergic receptors coupling with, electroconvulsive shock effect on, in brain)
- IT Brain, composition
 (cerebral cortex, .beta.-adrenergic-G protein-adenylate cyclase system of, electroconvulsive shock effect on)
- IT Convulsion
 (electro-, .beta.-adrenergic receptor-G protein-adenylate cyclase coupling response to, in brain)
- IT Receptors
 RL: BIOL (Biological study)
 (.beta.-adrenergic, G protein-adenylate cyclase coupling to, electroconvulsive shock effect on, in brain)
- IT **9012-42-4, Adenylate cyclase**
 RL: BIOL (Biological study)
 (.beta.-adrenergic receptor-G protein coupling with, electroconvulsion effect on, in brain)
- L76 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
 AN 1991:40359 HCAPLUS
 DN 114:40359
 TI Chronic electroconvulsive treatment augments coupling of the GTP-binding protein Gs to the catalytic moiety of **adenylyl cyclase** in a manner similar to that seen with chronic **antidepressant** drugs
- AU Ozawa, Hiroki; **Rasenick, Mark M.**
 CS Coll. Med., Univ. Illinois, Chicago, IL, 60680, USA
 SO J. Neurochem. (1991), 56(1), 330-8
 CODEN: JONRA9; ISSN: 0022-3042
 DT Journal
 LA English
 CC 14-10 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 1
- AB A significant increase of guanylylimidodiphosphate (GppNHp)-, fluoride-, and forskolin-stimulated **adenylyl cyclase** was obsd. in synaptic membrane preps. from rat cerebral cortex subsequent to chronic electroconvulsive shock (ECS) treatment. This effect required at least five treatments over a course of 10 days. The inhibition of **adenylyl cyclase** induced by GppNHp was not affected by these treatments. The disson. const. (kD) and maximal binding for the photoaffinity GTP analog. [32P]P3-(4-azidoanilido)-P1-5'-GTP([32P]AAGTP), to each of the synaptic membrane **G proteins** also were unchanged after ECS treatment. Nonetheless, the transfer of [32P]AAGTP from Gi to Gs, which the authors suggest is indicative of the coupling between Gs and the **adenylyl cyclase** catalytic moiety, was accelerated by chronic ECS treatment but not by acute or sham treatment. Furthermore, chem. uncoupling of Gs from **adenylyl cyclase** rendered membranes from treated animals indistinguishable from controls. Finally, in all cases tested, membranes prepd. from animals subjected to chronic treatment with amitriptyline or iprindole showed similar changes in the Gs-mediated activation of **adenylyl cyclase**. Acute treatments produced effects similar to controls, and liver and kidney membranes from animals receiving chronic treatment showed no changes in **adenylyl cyclase** despite the marked changes seen in brain. These results suggest that chronic administration of ECS enhances coupling between Gs, and **adenylyl cyclase** enzyme and modifies interactions between Gs and Gi.
- ST **adenylyl cyclase binding G protein**
 electroconvulsion; **antidepressant adenylyl cyclase binding G protein**
- IT Synapse

- (adenylyl cyclase binding by G proteins in membranes of, electroconvulsion and antidepressant drugs effects on)
- IT **Antidepressants**
(adenylyl cyclase of synaptic membranes response to electroconvulsion and, mechanism of action in relation to)
- IT Phospholipoproteins
RL: BIOL (Biological study)
(adenylate cyclase-inhibiting, guanine nucleotide-binding, Gi, Gs proteins interactions with, in synaptic membranes, electroconvulsion effect on, mechanism of action of antidepressant drugs in relation to)
- IT **Proteins, specific or class**
RL: BIOL (Biological study)
(adenylate cyclase-stimulating, guanine nucleotide-binding, Gs, adenylyl cyclase binding by, electroconvulsion and antidepressant drugs effects on)
- IT Convulsion
(electro-, G protein binding to adenylyl cyclase induced by, in synaptic membranes, mechanism of action of antidepressant drugs in relation to)
- IT **9012-42-4, Adenylyl cyclase**
RL: BIOL (Biological study)
(Gs proteins binding of, in synaptic membranes, electroconvulsion effect on, mechanism of antidepressant drugs in relation to)
- IT 50-47-5, Desipramine 50-48-6, Amitriptyline 5560-72-5, Iprindole
RL: BIOL (Biological study)
(adenylyl cyclase of synaptic membranes response to electroconvulsion and, mechanism of action in relation to)

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L114 ANSWER 1 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:158317 BIOSIS
DN PREV200200158317
TI Association of **Gsalpha** with membrane and cytoskeletal components is modified by chronic **antidepressant** treatment.
AU **Donati, Robert J. (1); Thukral, Chandreshekar (1); Rasenick, Mark M.**
CS (1) Physiology and Biophysics, University of Illinois, 835 S. Wolcott, Rm. No. E202, Chicago, IL, 60612 USA
SO Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 412a. <http://www.molbiolcell.org/>. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology Washington DC, USA December 08-12, 2001
ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Biophysics - Membrane Phenomena *10508
 Enzymes - General and Comparative Studies; Coenzymes *10802
 Pathology, General and Miscellaneous - Therapy *12512
 Pharmacology - General *22002

Pharmacology - Psychopharmacology *22026

- IT Major Concepts
 - Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Pharmacology
- IT Parts, Structures, & Systems of Organisms
 - cytoskeleton; plasma membrane
- IT Chemicals & Biochemicals
 - G-s-**alpha**; **adenylyl cyclase**: activation;
 - desipramine: **antidepressant** - drug, chronic treatment;
 - tubulin
- IT Miscellaneous Descriptors
 - Triton X-100 insoluble membrane domain; Triton X-100 soluble membrane domain; Meeting Abstract
- RN **9012-42-4 (ADENYLYL CYCLASE)**
 50-47-5 (DESIPRAMINE)

L114 ANSWER 2 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2002:155052 BIOSIS

DN PREV200200155052

TI **Antidepressant**-induced changes in **Gsalpha** cellular localization may be caused by a disruption of the plasma membrane lipid domain.

AU Donati, Robert J. (1); Thukral, Chandrashekar S.; Shah, Bindu N.; Rasenick, Mark M.

CS (1) Physiology and Biophysics, University of Illinois at Chicago, 835 S. Wolcott, Chicago, IL, 60612 USA

SO Molecular Biology of the Cell, (Dec., 2000) Vol. 11, No. Supplement, pp. 340a. <http://www.molbiolcell.org/>. print.
 Meeting Info.: 40th American Society for Cell Biology Annual Meeting San Francisco, CA, USA December 09-13, 2000
 ISSN: 1059-1524.

DT **Conference**

LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**

Cytology and Cytochemistry - General *02502

Biochemical Studies - General *10060

Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Biochemical Studies - Lipids *10066

Biochemical Studies - Sterols and Steroids *10067

Physiology, General and Miscellaneous - General *12002

Pathology, General and Miscellaneous - Therapy *12512

Pharmacology - General *22002

Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

- IT Major Concepts
 - Biochemistry and Molecular Biophysics; Cell Biology; Chemical Coordination and Homeostasis; Pharmacology
- IT Parts, Structures, & Systems of Organisms
 - Golgi
- IT Chemicals & Biochemicals
 - G-proteins**: analysis, functions, structures;
 - Gs-alpha proteins**: analysis, cellular localization changes; cholesterol; cyclodextrins; imipramine: adrenergic antagonist - drug, **antidepressant** - drug, autonomic - drug, pharmacodynamics; lipids; plasma membrane lipids: analysis, domain disruption, functions, structures; sphingolipids
- IT Miscellaneous Descriptors
 - signaling; Meeting Abstract
- RN 57-88-5 (CHOLESTEROL)
 12619-70-4 (CYCLODEXTRINS)
 50-49-7 (IMIPRAMINE)

L114 ANSWER 3 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:562372 BIOSIS

DN PREV200100562372

TI **Gsalpha** is a specific target of chronic **antidepressant** treatment.

AU **Donati, R. J. (1); Thukral, C. (1); Rasenick, M. M. (1)**

CS (1) Physiology and Biophysics, University of Illinois College of Medicine, Chicago, IL USA

SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1767. print.

Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001

ISSN: 0190-5295.

DT **Conference**

LA English

SL English

AB Previous studies in this laboratory have demonstrated that **Gsalpha** from C6 rat glioma cells migrates from a Triton X-100 (TTX-100) insoluble membrane domain (TIMD) to a TTX-100 soluble membrane domain in response to chronic treatment with the **antidepressants** desipramine and fluoxetine (Toki et al., 1999 J. Neurochem. 73(3): 1114-1120). In this same study it was also reported that there was a 50% decrease in the amount of **Gsalpha** localized to caveolae-enriched TTX-100 insoluble membranes. Laser scanning confocal microscopy revealed that **Gsalpha** is localized to the plasma membrane as well as the cytosol in both the desipramine-treated and control cells. However, striking differences were seen in the distribution of **Gsalpha** in the long cellular processes and process tips (Donati et al., 2001 Mol. Pharm. in press). There was no change in the distribution of **Gsalpha** after desipramine treatment. Current studies have focused on examining the localization of other members of the **Gsalpha** signaling cascade to TIMDs before and after desipramine treatment. These results indicate that while there is a 30-40% decrease in **Gsalpha** localized to these membrane domains, the localization of other members of the signaling cascade (**adenylyl cyclase type V/VI**, PKA II regulatory and catalytic subunits, and tubulin) remained relatively unchanged. This suggests that **antidepressant**-induced changes in the association of **Gsalpha** with the plasma membrane may be specific to this signal transducing protein and that **Gsalpha** may be a unique target of **antidepressant** action.

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520**

Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General *10060

Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Pathology, General and Miscellaneous - Therapy *12512

Nervous System - Physiology and Biochemistry *20504

Nervous System - Pathology *20506

Pharmacology - General *22002

Pharmacology - Psychopharmacology *22026

Neoplasms and Neoplastic Agents - Pathology; Clinical Aspects; Systemic Effects *24004

BC Muridae 86375

IT Major Concepts

Nervous System (Neural Coordination); Pharmacology

IT Parts, Structures, & Systems of Organisms

caveola; cytosol; plasma membrane

IT Diseases

glioma: neoplastic disease, nervous system disease

IT Chemicals & Biochemicals

Gs-alpha: distribution, localization, signaling;

PKA II [protein kinase A II]: catalytic subunit, localization, regulatory subunit; Triton X-100 insoluble membrane domain [TIMD];

Triton X-100 soluble membrane domain; **adenylyl**

cyclase type V/VI: localization;

desipramine: **antidepressant** - drug, pharmacodynamics;
tubulin: localization

IT Alternate Indexing
Glioma (MeSH)

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
C6 cell line (Muridae): rat glioma cell

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates

RN 50-47-5 (DESIPRAMINE)

L114 ANSWER 4 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:478361 BIOSIS
DN PREV200100478361
TI Alterations in the distribution of **G protein** in the
plasma membrane from postmortem brains of **depressive** and
schizophrenic.

AU **Toki, S. (1)**; Senda, S.; Ozawa, H. (1); Choei, H. (1); Yamada,
S. (1); Saito, T. (1)

CS (1) Neuropsychiatry, Sapporo Medical Univ, Sapporo Japan
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 310. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San
Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.

DT **Conference**
LA English
SL English

AB Previous study have suggested that the altered function in the
second-messenger system may involve in the etiology of psychiatric
disorders. In **depressives**, the attenuation of the **Gs**
-mediated **adenylyl cyclase** (AC) activity in the
cerebral cortex has been suggested. On the other hand, several
investigators have reported the increased AC activity in the brain from
the schizophrenics. Recently, it has been suggested that the membrane
proteins such as **G proteins** and receptors are
associated with some cytoskeletal **proteins** that restrict the
distribution and mobility of these **proteins** and alteration in
the interaction between these components might affect to the
second-messenger system. Therefore, we examined the alteration in the
distribution of **G proteins** in the plasma membrane from
postmortem human brains of patients with psychiatric disorders. Frontal
cortex membranes from the post-mortem brains of **depressives**,
schizophrenics and controls were examined. Membrane-enriched fractions
from each group were prepared from frontal cortex and membrane
proteins were extracted with detergent (Triton X-100 (TX-100)).
The amount of **G protein** in each extract was estimated
by immunoblotting. In **depressive** group, TX-100 extracted less
amount of **G(s alpha)** from the membrane in compare to
control group. On the other hand, in the schizophrenic group, TX-100
extracted more **G(s alpha)** from the membrane in compare
to control group. These change might affect to the coupling between
G protein and effector. Therefore, these data suggests
that the change in the distribution of **G protein** may
involve in the etiology of psychiatric disorders.

CC **General Biology - Symposia, Transactions and Proceedings of**
Conferences, Congresses, Review Annuals *00520
Cytology and Cytochemistry - Human *02508
Behavioral Biology - General and Comparative Behavior *07002
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Membrane Phenomena *10508
Enzymes - General and Comparative Studies; Coenzymes *10802

Nervous System - Physiology and Biochemistry *20504

BC Hominidae 86215

IT Major Concepts
Behavior; Membranes (Cell Biology); Nervous System (Neural Coordination)

IT Parts, Structures, & Systems of Organisms
brain: histology, nervous system; cerebral cortex: nervous system; cytoskeleton; frontal cortex: nervous system; plasma membrane

IT Diseases
depression: behavioral and mental disorders; schizophrenia: behavioral and mental disorders

IT Chemicals & Biochemicals
G protein: distribution, membrane **protein**, mobility; **adenylyl cyclase**

IT Alternate Indexing
Depression (MeSH); Schizophrenia (MeSH)

IT Methods & Equipment
autopsy: evaluation method

IT Miscellaneous Descriptors
second messenger system; Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): cadaver, patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 9012-42-4 (ADENYLYL CYCLASE)

L114 ANSWER 5 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:297741 BIOSIS

DN PREV200100297741

TI Chronic treatment of C6 glioma cells with **antidepressant** drugs results in a redistribution of **G α** .

AU Donati, Robert J.; Thukral, Chandrashekhar; Rasenick, Mark M. (1)

CS (1) Department of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, 835 S. Wolcott Ave., Rm. E202, Chicago, IL, 60612-7342: raz@uic.edu USA

SO Molecular Pharmacology, (June, 2001) Vol. 59, No. 6, pp. 1426-1432. print. ISSN: 0026-895X.

DT Article

LA English

SL English

AB Previous studies have demonstrated that chronic treatment of C6 glioma cells with the **antidepressants** desipramine and fluoxetine increases the Triton X-100 solubility of the **G protein G α** (Toki et al., 1999). The **antidepressants** also caused a 50% decrease in the amount of **G α** localized to caveolae-enriched membrane domains. In this study, laser scanning confocal microscopy reveals that **G α** is localized to the plasma membrane as well as the cytosol in both treated and control cells. However, striking differences are seen in the distribution of **G α** in the long cellular processes after chronic treatment with these **antidepressant** drugs. Control cells display **G α** along the entire process with an especially high concentration of that **G protein** at the distal ends. Desipramine- or fluoxetine-treated cells show a more centralized clustering of **G α** in the Golgi region of the cell and a drastic reduction of **G α** in the cellular processes. There is no change in the distribution of **G α** after desipramine treatment and the antipsychotic drug chlorpromazine does not alter **G α** . These results suggest that **antidepressant**-induced changes in the association of **G α** with the plasma membrane may translate into altered cellular localization of this signal transducing **protein**. Thus, modification of the coupling between **Gs**-coupled receptors and **adenylyl cyclase** may

underlie both **antidepressant** therapy and **depressive** illnesses. This report also suggests that modification of the membrane domain occupied by **Gsalpha** might represent a mechanism for chronic **antidepressant** effects.

CC Enzymes - General and Comparative Studies; Coenzymes *10802
 Cytology and Cytochemistry - Animal *02506
 Biochemical Studies - General *10060
 Biophysics - Membrane Phenomena *10508
 Pathology, General and Miscellaneous - Therapy *12512
 Nervous System - Physiology and Biochemistry *20504
 Pharmacology - General *22002
Pharmacology - Psychopharmacology *22026

BC Muridae 86375

IT Major Concepts
 Membranes (Cell Biology); Nervous System (Neural Coordination);
 Pharmacology

IT Parts, Structures, & Systems of Organisms
 Golgi region; caveolae-enriched membrane domains; cellular processes;
 cytosol; plasma membrane

IT Diseases
depression: behavioral and mental disorders

IT Chemicals & Biochemicals
Gs-alpha: G protein,
 redistribution; **adenyl cyclase**;
antidepressant drugs; chlorpromazine: antipsychotic - drug;
 desipramine: **antidepressant** - drug; fluoxetine:
antidepressant - drug

IT Alternate Indexing
Depression (MeSH)

IT Methods & Equipment
 chronic drug treatment: therapeutic method; laser scanning confocal
 microscopy: microscopy method

IT Miscellaneous Descriptors
 signal transduction

ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 C6 cell line (Muridae): rat glioma cells

ORGN Organism Superterms
 Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
 Rodents; Vertebrates

RN **9012-42-4 (ADENYL CYCLASE)**
 50-53-3 (CHLORPROMAZINE)
 50-47-5 (DESIPRAMINE)
 54910-89-3 (FLUOXETINE)

L114 ANSWER 6 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:135070 BIOSIS
 DN PREV200100135070
 TI Serotonin induces MAPK activation in primary cultures of cortical neurons.
 AU Tolbert, L. M. (1); Duman, R. S.
 CS (1) Yale University, New Haven, CT USA
 SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract
 No.-868.14. print.
 Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New
 Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
 . ISSN: 0190-5295.

DT **Conference**
 LA English
 SL English

AB Although most classes of **antidepressants** act by increasing
 synaptic levels of serotonin and/or norepinephrine, the delayed
 therapeutic action of these drugs cannot be explained by their immediate
 effects. Two hypotheses have been proposed to explain the long-term
 changes in target neurons of serotonergic projections that may occur with
 long-term **antidepressant** treatment. Our lab has demonstrated

that chronic **antidepressant** administration upregulates several components of cAMP cascade, including the transcription factor CREB. Thus, CREB-mediated changes in gene expression could account for long-term adaptive changes underlying **antidepressant** action. Alternatively, the work of de Montigny et al. reveals that chronic **antidepressant** administration results in a progressive sensitization of post-synaptic 5-HT_{1A} receptors, which are negatively coupled to **adenylyl cyclase** via the **G protein**, Gi. These seemingly contradictory findings can potentially be rationalized by the involvement of the MAPK cascade in 5-HT_{1A} receptor signalling. Previous studies have shown that MAPK can induce CREB phosphorylation indirectly via the Rsk family of **protein** kinases. We have shown previously that serotonin and norepinephrine induce CREB phosphorylation in primary cultures of rat cortical neurons. Now we demonstrate that both 5-HT and NE induce MAPK phosphorylation with a similar time course. We have found that norepinephrine-induced MAPK activation is blocked by the **alpha1** antagonist prazosin, but is unaffected by the non-selective beta antagonist propranolol. We are currently investigating the contribution of the 5-HT_{1A} receptor and other 5-HT receptor subtypes to MAPK activation using subtype-specific antagonists. Furthermore, we are studying the relationship between MAPK activation and CREB phosphorylation in order to elucidate the role of MAPK in CREB activation.

- CC **Pharmacology - Psychopharmacology *22026**
General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals *00520
 Cytology and Cytochemistry - Animal *02506
 Behavioral Biology - General and Comparative Behavior *07002
 Behavioral Biology - Animal Behavior *07003
 Biochemical Studies - General *10060
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Pathology, General and Miscellaneous - Therapy *12512
 Endocrine System - Neuroendocrinology *17020
 Nervous System - Physiology and Biochemistry *20504
 Pharmacology - General *22002
- BC Muridae 86375
- IT Major Concepts
 Behavior; Nervous System (Neural Coordination); Pharmacology
- IT Parts, Structures, & Systems of Organisms
 cortical neuron: nervous system
- IT Chemicals & Biochemicals
 5-HT-1-A receptor; CREB: phosphorylation; MAPK: activation;
antidepressants: antidepressant; norepinephrine;
 serotonin
- IT Miscellaneous Descriptors
 Meeting Abstract
- ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 rat (Muridae)
- ORGN Organism Superterms
 Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
 Rodents; Vertebrates
- RN 51-41-2 (NOREPINEPHRINE)
 50-67-9 (SEROTONIN)
- L114 ANSWER 7 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:131847 BIOSIS
 DN PREV200100131847
 TI Alterations in the detergent extraction of **G protein**
 from the plasma membrane from postmortem human brains of patients with
depression.
- AU Senda, S. (1); Toki, S.; Ozawa, H.; Choei, H.; Yamada, S.;
 Riederer, P.; Saito, T.
- CS (1) Sapporo Medical Univ, Sapporo Japan
- SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract

No.-866.8. print.

Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
 . ISSN: 0190-5295.

DT **Conference**

LA English

SL English

AB Previous studies have suggested that attenuation of the **Gs**-mediated **adenylyl cyclase** (AC) activity in the cerebral cortex may be involved in the etiology of **depression**. Recently, it has been suggested that membrane **proteins** such as receptors, **G proteins** and effectors are associated with some cytoskeletal **proteins** that restrict the distribution and mobility of these **proteins** to a surprising degree. Furthermore, Toki et al. (1999) reported that the change in the distribution of **Gs alpha** in the plasma membrane caused by chronic **antidepressant** treatment affects the **G protein**-mediated AC activity. Therefore, in the present study, we examined the alteration in the distribution of **G proteins** in the plasma membrane from postmortem human brains of patients with **depression** and age-matched controls by the detergent extraction method. Tissue samples were obtained from nine unipolar **depressives** and nine controls. A membrane-enriched fraction was prepared from frontal cortex and stirred in ice-cold HEPES (15 muM, pH 7.4) containing 1% Triton X-100 (TX-100) for 60 min followed by centrifugation at 100,000 **g** for 60 min at 4degree C. The supernatant and pellet were collected and the amount of **Gs alpha** in each fraction was estimated by immunoblotting. TX-100 extracted less **Gs alpha** from the **depressive** group than from the control group and more **Gs alpha** remained in the pellet in the **depressive** group than in the control group. These data suggest that there is more **Gs alpha** in the strongly hydrophobic portion of the synaptic membrane in the **depressive** group than that in controls. Therefore, a change in the distribution of **G protein** may be involved in the etiology of **depression**.

CC Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
 Behavioral Biology - Human Behavior *07004
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Nervous System - Physiology and Biochemistry *20504
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

BC Hominidae 86215

IT Major Concepts

Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms

cerebral cortex: nervous system; plasma membrane

IT Diseases

depression: behavioral and mental disorders

IT Chemicals & Biochemicals

G protein; adenylyl cyclase

IT Alternate Indexing

Depression (MeSH)

IT Methods & Equipment

immunoblotting: analytical method; postmortem examination: analytical method

IT Miscellaneous Descriptors

Meeting Abstract

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae): patient

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates
 RN 9012-42-4 (ADENYLYL CYCLASE)

L114 ANSWER 8 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:131846 BIOSIS
 DN PREV200100131846
 TI cAMP and inositol phosphates related signal transduction in
depressions and schizophrenia.
 AU Ozawa, H. (1); Yamaguchi, T.; Senda, S.; Toki, S.; Choiei, H.;
 Yamada, S.; Riederer, P.; Saito, T.
 CS (1) Sapporo Medical University, Sapporo Japan
 SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract
 No.-866.7. print.
 Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New
 Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
 . ISSN: 0190-5295.

DT **Conference**
 LA English
 SL English
 AB Mood disorders and schizophrenia are the two most important endogenous
 psychiatric diseases. Recently several researchers have suggested that
 there are common and overlapping symptoms between these two disorders.,
 especially in terms of **depression** and negative symptoms of
 chronic schizophrenia. In the present study, we examined the productive
 activity of two second messengers systems (**adenylyl**
cyclase (AC) which produces cAMP and phospholipase C (PLC) which
 produces Inositol phosphates (Ips)) in membrane preparations from
 postmortem frontal cortex of unipolar **depressive** patients
 without manic episodes. (11 patients AGE : 68.6+-3.5y, PMDT:
 19.6+-10.1hr) and chronic schizophrenia (11 patients AGE : 67.3+-3.5y,
 PMDT: 10.8+-3.1hr) in comparison with control subjects (10 subjects AGE :
 79.0 +-3.1y, PMDT: 10.0+- 3.58hr). Basal AC activity was significantly
 decreased in **depressives**, and Mn2+- **stimulated** AC
 activity had a tendency to decline compared to controls. In contrast to
depressions, there were no differences in basal and Mn2+
stimulated AC activity between schizophrenia and controls. In the
 other hand, 5-HT-**stimulated** PLC activity was significantly
 increased in both **depressives** and schizophrenia compared to
 controls. These results indicated that the enhancement in 5HT2 receptor
 regulated IPs productions is related to the pathophysiology of both
depression and chronic schizophrenia.

CC Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals *00520
 Behavioral Biology - Human Behavior *07004
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Endocrine System - Neuroendocrinology *17020
 Nervous System - Physiology and Biochemistry *20504
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

BC Hominidae 86215
 IT Major Concepts
 Neurology (Human Medicine, Medical Sciences); Psychiatry (Human
 Medicine, Medical Sciences)
 IT Parts, Structures, & Systems of Organisms
 frontal cortex: nervous system
 IT Diseases
depression: behavioral and mental disorders; manic episodes:
 behavioral and mental disorders, nervous system disease; mood disorder:
 behavioral and mental disorders, nervous system disease; schizophrenia:
 behavioral and mental disorders, negative symptoms, nervous system
 disease
 IT Chemicals & Biochemicals
adenylyl cyclase; cyclic AMP; inositol phosphates;
 phospholipase C; serotonin; serotonin type II receptor

IT Alternate Indexing
Depression (MeSH); Mood Disorders (MeSH); Schizophrenia (MeSH)

IT Miscellaneous Descriptors
 signal transduction; Meeting Abstract

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae): patient

ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
 60-92-4 (CYCLIC AMP)
 15421-51-9Q (INOSITOL PHOSPHATES)
 68247-19-8Q (INOSITOL PHOSPHATES)
 9001-86-9 (PHOSPHOLIPASE C)
 50-67-9 (SEROTONIN)

L114 ANSWER 9 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:110540 BIOSIS

DN PREV200100110540

TI Chronic **antidepressant** treatment alters the cellular localization of **Gsalpha**.

AU **Donati, R. J. (1); Rasenick, M. M.**

CS (1) University of Illinois College of Medicine, Chicago, IL USA

SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-387.15. print.
 Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.

DT **Conference**

LA English

SL English

AB Previous studies in this laboratory have demonstrated that **Gsalpha** from C6 rat glioma cells migrates from a Triton X-100 (TTX-100) insoluble membrane domain to a TTX-100 soluble membrane domain in response to chronic treatment with the **antidepressants** desipramine and fluoxetine (Toki et al., 1999 J. Neurochem. 73(3): 1114-1120). In this same study it was also reported that there was a 50% decrease in the amount of **Gsalpha** localized to caveolae-enriched TTX-100 insoluble membranes. Current studies have focused on visualizing this pattern of **Gsalpha** movement using laser scanning confocal microscopy. **Gsalpha** is localized to the plasma membrane as well as the cytosol in both the treated and control cells. However, striking differences are seen in the distribution of **Gsalpha** in the long cellular processes. Control cells express **Gsalpha** along the entire process with a high concentration at the distal end while desipramine treated cells show a more centralized clustering of **Gsalpha** in the Golgi region of the cell. Furthermore, the appearance of **Gsalpha** in the processes is drastically reduced in the treated cells. There is no change in the distribution of **Gsalpha** after desipramine treatment. Fluoxetine also induces the transfer of **Gsalpha**, however the number of cells observed with this pattern of relocation is fewer than that seen with desipramine. These results suggest that **antidepressant**-induced changes in the association of **Gsalpha** with the plasma membrane may translate into altered cellular localization of this signal transducing protein.

CC Pharmacology - General *22002
 General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
 Cytology and Cytochemistry - General *02502
 Cytology and Cytochemistry - Animal *02506
 Behavioral Biology - General and Comparative Behavior *07002
 Behavioral Biology - Animal Behavior *07003
 Biochemical Studies - General *10060
 Pathology, General and Miscellaneous - Therapy *12512

Nervous System - Physiology and Biochemistry *20504
Pharmacology - Psychopharmacology *22026

BC Muridae 86375
IT Major Concepts
Behavior; Cell Biology; Nervous System (Neural Coordination);
Pharmacology

IT Parts, Structures, & Systems of Organisms
cytosol; plasma membrane

IT Chemicals & Biochemicals
Gs-alpha: cellular localization alteration, signal
transducing protein; Triton X-100 insoluble membranes; desipramine:
antidepressant - drug, chronic treatment; fluoxetine:
antidepressant - drug, chronic treatment

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
C6 cell line (Muridae): rat glioma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates

RN 50-47-5 (DESIPRAMINE)
54910-89-3 (FLUOXETINE)

L114 ANSWER 10 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:83580 BIOSIS
DN PREV200000083580
TI Both the membrane association and cellular localization of Gsalpha
are altered by antidepressant treatment.

AU Donati, Robert J. (1); Rasenick, Mark M. (1)
CS (1) University of Illinois at Chicago, 835 S. Wolcott, Chicago, IL, 60612
USA

SO Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 419a.
Meeting Info.: 39th Annual Meeting of the American Society for Cell
Biology Washington, D.C., USA December 11-15, 1999 The American Society
for Cell Biology
. ISSN: 1059-1524.

DT Conference
LA English
CC Biophysics - Membrane Phenomena *10508
Cytology and Cytochemistry - Animal *02506
General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals *00520

BC Muridae 86375
IT Major Concepts
Membranes (Cell Biology)

IT Parts, Structures, & Systems of Organisms
membrane

IT Chemicals & Biochemicals
G-s-alpha: localization; Triton X-100;
antidepressants; caveolin

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
C6 cell line (Muridae): rat glioma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates

RN 9002-93-1 (TRITON X-100)

L114 ANSWER 11 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:451149 BIOSIS
DN PREV199900451149

TI Treatment of C6 glioma cells and rats with **antidepressant** drugs increases the detergent extraction of **Gsalpha** from plasma membrane.

AU **Toki, Sadamu; Donati, Robert J.; Rasenick, Mark M. (1)**

CS (1) Department of Physiology and Biophysics, University of Illinois College of Medicine, 835 S. Wolcott Avenue, Chicago, IL, 60612-7342 USA

SO Journal of Neurochemistry, (Sept., 1999) Vol. 73, No. 3, pp. 1114-1120. ISSN: 0022-3042.

DT Article

LA English

SL English

AB Results from previous studies suggested that chronic treatment of rats or C6 glioma cells with **antidepressants** augments the coupling between **Gs** and **adenylyl cyclase**. As these effects on C6 glioma cells are seen in the absence of presynaptic input, several **antidepressant** drugs may have a direct "postsynaptic" effect on their target cells. It was hypothesized that the target of **antidepressant** action was some membrane **protein** that may regulate coupling between **G proteins** and **adenylyl cyclase**. To test this, C6 glioma cells were treated with amitriptyline, desipramine, iprindole, or fluoxetine for 3 days. Chlorpromazine served as a control for these treatments. Membrane **proteins** were extracted sequentially with Triton X-100 and Triton X-114 from C6 glioma cells. Triton X-100 extracted more **Gsalpha** in membranes prepared from **antidepressant**-treated C6 glioma cells than from control groups. In addition, cell fractionation studies revealed that the amount of **Gsalpha** in caveolin-enriched domains was reduced after **antidepressant** treatment and that **adenylyl cyclase** comigrated with **Gsalpha** in the gradients. These data suggest that some postsynaptic component that increases availability of **Gs** to activate effector molecules, such as **adenylyl cyclase**, might be a target of **antidepressant** treatment.

CC Pharmacology - General *22002
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Biophysics - Membrane Phenomena *10508
Enzymes - General and Comparative Studies; Coenzymes *10802
Metabolism - General Metabolism; Metabolic Pathways *13002
Nervous System - General; Methods *20501
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

BC Muridae 86375

IT Major Concepts
Cell Biology; Nervous System (Neural Coordination); Pharmacology

IT Parts, Structures, & Systems of Organisms
plasma membrane: blood and lymphatics

IT Chemicals & Biochemicals
adenylyl cyclase; amitriptyline:
antidepressant - drug; chlorpromazine: **antidepressant**
- drug; desipramine: **antidepressant** - drug; fluoxetine:
antidepressant - drug; iprindole: **antidepressant** -
drug; **G protein**; **G-s alpha**:
detergent extraction

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae); C6 cell line (Muridae): rat glioma cells

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)
54910-89-3 (FLUOXETINE)

50-53-3 (CHLORPROMAZINE)

L114 ANSWER 12 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1999:447949 BIOSIS
 DN PREV199900447949
 TI **G protein**-coupled cyclic AMP signaling in postmortem brain of subjects with mood disorders: Effects of diagnosis, suicide, and treatment at the time of death.
 AU Dowlatshahi, Dar; MacQueen, Glenda M.; Wang, Jun-Feng; Reiaich, James S.; Young, L. Trevor (1)
 CS (1) Department of Psychiatry and Behavioural Neurosciences, McMaster University, HSC-4N77A, 1200 Main St. W., Hamilton, ON, L8N 3ZS Canada
 SO Journal of Neurochemistry, (Sept., 1999) Vol. 73, No. 3, pp. 1121-1126. ISSN: 0022-3042.
 DT Article
 LA English
 SL English
 AB Components of cyclic AMP (cAMP) signaling were examined in postmortem cerebral cortex of a well characterized group of patients with mood disorders and nonpsychiatric control subjects. We measured **G protein** levels, **adenylyl cyclase** (AC) activity, and CREB levels in cerebral cortex of the subjects with respect to diagnosis, treatment, and suicide. There was no effect of diagnosis on any measure, except for a trend toward decreased **stimulated** AC activity in subjects with mood disorders relative to control subjects. We also detected a significant effect of suicide on temporal cortex CREB levels in subjects that died as a result of suicide relative to those that did not, which was more evident in patients with major **depressive** disorder. Bipolar disorder (BD) subjects treated with anticonvulsants at the time of death had decreased temporal cortex CREB levels relative to those not receiving anticonvulsants. Furthermore, we found a trend toward decreased occipital cortex **Galphas** (short) levels in BD subjects treated with lithium. These results support the hypothesis of altered cAMP signaling in mood disorders and raise the possibility that factors other than diagnosis, such as treatment and suicide, may be relevant to cell-signaling abnormalities reported in the literature.
 CC Nervous System - General; Methods *20501
 Biochemical Studies - General *10060
 Enzymes - General and Comparative Studies; Coenzymes *10802
 Pathology, General and Miscellaneous - Diagnostic *12504
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pathology, General and Miscellaneous - Therapy *12512
 Metabolism - General Metabolism; Metabolic Pathways *13002
 BC Hominidae 86215
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences)
 IT Parts, Structures, & Systems of Organisms
 brain: nervous system, postmortem; cerebral cortex: nervous system; occipital cortex: nervous system
 IT Diseases
 bipolar disorder: behavioral and mental disorders; mood disorder: behavioral and mental disorders, treatment, diagnosis; suicide: behavioral and mental disorders
 IT Chemicals & Biochemicals
adenylyl cyclase: activity; cyclic AMP: signaling; CREB [cyclic AMP-response element binding **protein**]; **G protein**; **G protein**-coupled cyclic AMP: signaling
 IT Alternate Indexing
 Bipolar Disorder (MeSH); Mood Disorders (MeSH); Suicide (MeSH)
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 60-92-4 (CYCLIC AMP)
9012-42-4 (ADENYLYL CYCLASE)

L114 ANSWER 13 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:80153 BIOSIS
DN PREV199900080153
TI Modification of the interaction between **G protein** and
the cytoskeleton after chronic **antidepressant** treatment.
AU **Toki, S.; Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 1490.
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 2
Los Angeles, California, USA November 7-12, 1998
ISSN: 0190-5295.
DT **Conference**
LA English
CC Nervous System - General; Methods *20501
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Pharmacology - General *22002
**General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals *00520**
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural
Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
cytoskeleton; presynaptic membranes
IT Chemicals & Biochemicals
adenylyl cyclase; amitriptyline:
antidepressant - drug; fluoxetine: antidepressant -
drug; iprindole: antidepressant - drug; G
protein
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae); C6 cell line (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates
RN 9012-42-4 (ADENYLYL CYCLASE)
50-48-6 (AMITRIPTYLINE)
54910-89-3 (FLUOXETINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 14 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:533807 BIOSIS
DN PREV199799833010
TI Chronic **antidepressant** treatment alters the interaction between
G proteins and the cytoskeleton.
AU **Toki, S.; Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
SO Society for Neuroscience Abstracts, (1997) Vol. 23, No. 1-2, pp. 2232.
Meeting Info.: 27th Annual Meeting of the Society for Neuroscience New
Orleans, Louisiana, USA October 25-30, 1997
ISSN: 0190-5295.
DT **Conference; Abstract; Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802

Nervous System - General; Methods *20501
 Pharmacology - General *22002
 BC Muridae *86375
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology; Enzymology
 (Biochemistry and Molecular Biophysics); Nervous System (Neural
 Coordination); Pharmacology
 IT Chemicals & Biochemicals
 ADENYLYL CYCLASE; AMITRIPTYLINE; IMIPRAMINE;
 IPRINDOLE
 IT Miscellaneous Descriptors
 ADENYLYL CYCLASE; AMITRIPTYLINE;
 ANTIDEPRESSANT-DRUG; **ANTIDEPRESSANTS**; CHRONIC
 ANTIDEPRESSANT TREATMENT; CYTOSKELETON; EXPERIMENTAL METHOD;
 G PROTEIN; IMIPRAMINE; IPRINDOLE; MEMBRANES; NERVOUS
 SYSTEM; PHARMACOLOGY; POST-SYNAPTIC EFFECT; SYNAPTIC MEMBRANES
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rat (Muridae)
 ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates
 RN **9012-42-4 (ADENYLYL CYCLASE)**
 50-48-6 (AMITRIPTYLINE)
 50-49-7 (IMIPRAMINE)
 5560-72-5 (IPRINDOLE)

L114 ANSWER 15 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1997:125196 BIOSIS
 DN PREV199799431699
 TI Genetic markers of alcohol abuse.
 AU Ferguson, Ralph A.; Goldberg, David M. (1)
 CS (1) Dep. Clinical Biochemistry, Banting Inst., Univ. Toronto, 100 Banting
 Street, Toronto, ON M5G 1L5 Canada
 SO Clinica Chimica Acta, (1997) Vol. 257, No. 2, pp. 199-250.
 ISSN: 0009-8981.
 DT General Review
 LA English
 AB In this paper, we review the current status of genetic markers for the
 development of alcohol abuse. Family, twin, half-sibling and adoption
 studies of alcoholic subjects suggest that the heritability of liability
 to alcoholism is at least 50%. These findings have fuelled intensive
 investigation in the fields of neurology, biochemistry, genetics and
 molecular biology aimed at the identification of markers for the risk of
 alcoholism. The most promising of these are discussed in detail. Alcohol
 dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) polymorphisms,
 specifically the ADH3*1, ADH2*2, and ALDH2*2 genotypes appear to confer a
 protective effect against alcoholism, most notably in Oriental subjects.
 Caucasian alcohol abusers and their first-degree relatives exhibit
 depressed platelet monoamine oxidase activity, the degree of which
 is greater in Type II than Type I alcoholics. Electrophysiological
 characteristics of alcoholics and those at risk for developing alcoholism
 have also been identified, including the reduced amplitude of the
 event-related brain potential and, after ethanol ingestion, characteristic
 EEG **alpha-wave** activity. Lower platelet **adenylate**
 cyclase activity is seen in alcoholics compared to controls,
 presumably as a result of over-expression of an inhibitory **G-**
 protein. Markers related to other signal transduction pathways of
 the central nervous system including the serotonergic, muscarinic and
 dopaminergic systems are also discussed. In this group of markers, the
 putative association between the inheritance of the A1 allele of the D2
 dopamine receptor and the susceptibility to alcoholism provides the most
 dramatic illustration of the challenges presently existing in this field
 of scientific investigation. Current limitations in the definition,
 diagnosis and classification of alcoholism, the confounding influences of

race and gender on association studies, as well as the statistical approach of linkage studies are discussed as they relate to the endeavor to uncover valid genetic markers for the risk of alcoholism.

- CC Genetics and Cytogenetics - Human *03508
 Genetics and Cytogenetics - Sex Differences *03510
 Social Biology; Human Ecology *05500
 Behavioral Biology - Human Behavior 07004
 Enzymes - Physiological Studies *10808
Psychiatry - Addiction - Alcohol, Drugs, Smoking, etc. *21004
 Toxicology - General; Methods and Experimental *22501
- BC Hominidae *86215
- IT Major Concepts
 Enzymology (Biochemistry and Molecular Biophysics); Genetics; Human Ecology (Anthropology); Psychiatry (Human Medicine, Medical Sciences); Toxicology
- IT Chemicals & Biochemicals
 ALCOHOL; ALCOHOL DEHYDROGENASE; ALDEHYDE DEHYDROGENASE
- IT Miscellaneous Descriptors
 ALCOHOL ABUSE; ALCOHOL DEHYDROGENASE; ALDEHYDE DEHYDROGENASE; BEHAVIOR; BEHAVIORAL AND MENTAL DISORDERS; ETHNIC DIFFERENCES; GENDER DIFFERENCES; GENETIC MARKERS; TOXICOLOGY
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 human (Hominidae)
- ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
- RN 64-17-5 (ALCOHOL)
 9031-72-5 (ALCOHOL DEHYDROGENASE)
 9028-86-8 (ALDEHYDE DEHYDROGENASE)
- L114 ANSWER 16 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1997:33767 BIOSIS
 DN PREV199799340170
 TI Regulation of signal transduction pathways by mood-stabilizing agents: Implications for the delayed onset of therapeutic efficacy.
 AU Manji, Hussein K. (1); Chen, Guang; Hsiao, John K.; Risby, Emile D.; Masana, Monica I.; Potter, William Z.
 CS (1) Schizophrenia Mood Disorders Clin. Res. Div., Dep. Psychiatr. Behavioral Neurosci., Wayne State Univ. Sch. Med., UHC 9B, 4201 St. Antoine Blvd., Detroit, MI 48201 USA
 SO Journal of Clinical Psychiatry, (1996) Vol. 57, No. SUPPL. 13, pp. 34-46. ISSN: 0160-6689.
 DT General Review
 LA English
 AB A series of investigations were performed to elucidate the mechanisms of action of lithium, valproate, and carbamazepine. We have found that lithium exerts major effects on **G proteins**, most likely via a posttranslational process stabilizing the inactive heterotrimeric (**alpha**-beta-gamma) form of the **protein**. We also find that chronic lithium and valproate exert major, very similar effects on the PKC signaling pathway, with both drugs decreasing the levels of membrane-associated PKC **alpha** and epsilon, and have similar effects on the DNA binding activity of the transcription factor, AP-1. By contrast, we find that carbamazepine exerts major, direct inhibitory effect at the level of **adenylyl cyclases**. Overall, the results suggest that signal transduction pathways are targets for the actions of mood-stabilizing agents; given their key roles in the amplification and integration of signals in the central nervous system, these findings have clear implications not only for research into the etiology/pathophysiology of manic-depressive illness, but also for the development of innovative treatment strategies.
- CC Cytology and Cytochemistry - Animal *02506
 Behavioral Biology - Human Behavior *07004
 Biochemical Studies - General 10060
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - Membrane Phenomena *10508
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Therapy *12512
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
 BC Hominidae *86215
 IT Major Concepts
 Behavior; Cell Biology; Enzymology (Biochemistry and Molecular
 Biophysics); Membranes (Cell Biology); Pathology; Pharmacology;
 Psychiatry (Human Medicine, Medical Sciences)
 IT Chemicals & Biochemicals
 LITHIUM; VALPROATE; CARBAMAZEPINE; PROTEIN KINASE C
 IT Miscellaneous Descriptors
 ANTIDEPRESSANT AGENTS; ANTIDEPRESSANT-DRUG;
 BEHAVIOR; BEHAVIORAL AND MENTAL DISORDERS; CARBAMAZEPINE; DELAYED
 ONSET; DELAYED ONSET OF ACTION; **G PROTEIN**; LITHIUM;
 MANIA; MOOD-STABILIZING AGENTS; PHARMACODYNAMICS; PHARMACOLOGY;
 PROTEIN KINASE C; SIGNAL TRANSDUCTION PATHWAY REGULATION;
 THERAPEUTIC EFFICACY; TREATMENT; VALPROATE
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae)
 ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
 RN 7439-93-2 (LITHIUM)
 99-66-1 (VALPROATE)
 298-46-4 (CARBAMAZEPINE)
 141436-78-4 (PROTEIN KINASE C)

 L114 ANSWER 17 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1997:23283 BIOSIS
 DN PREV199799322486
 TI Beta-Adrenoceptor-linked protein kinase A (PKA) activity in human
 fibroblasts from normal subjects and from patients with major
 depression.
 AU Manier, D. Hal; Eiring, Andrea; Shelton, Richard C.; Sulser, Fridolin (1)
 CS (1) Vanderbilt Univ. Sch. Med., AA-2232 MCN, Nashville, TN 37232 USA
 SO Neuropsychopharmacology, (1996) Vol. 15, No. 6, pp. 555-561.
 ISSN: 0893-133X.
 DT Article
 LA English
 AB Human fibroblasts from normal subjects and from patients with major
 depression are cultured and their beta-adrenoreceptor-cyclic AMP-
 protein kinase A (PKA) system characterized. The results indicate
 that the beta-adrenoreceptor-mediated activation of PKA in the 900
 g supernatant fraction of human fibroblasts is mediated via
 beta-adrenoreceptors. The activation of PKA by isoproterenol is very rapid
 with maximal **stimulation** occurring at 5 seconds. The time course
 of PKA activation by isoproterenol in fibroblasts from patients with major
 depression is identical to that in fibroblasts from normal
 subjects but the magnitude of activation is significantly reduced in
 fibroblasts from patients with major **depression**. Dose-response
 curves on cyclic AMP mediated activation of PKA confirmed the previously
 reported reduction in activation of PKA in patients with major
 depression but demonstrated that this reduction occurs without a
 change in the EC-50 values of cyclic AMP (approximately 20 nmol/L). The
 blunted beta-adrenoceptor-linked PKA responses in patients with major
 depression occur without a change in the expression of the PKA
 catalytic subunit C-**alpha**. The studies suggest that the
 beta-adrenoceptor-coupled **adenylate cyclase** PKA system
 in human fibroblasts may represent a valid model to explore possible
 abnormalities in the fine tuning of the beta-adrenergic transduction
 cascade in patients with affective disorders.
 CC Cytology and Cytochemistry - Human *02508

Behavioral Biology - Human Behavior *07004
 Biochemical Studies - General *10060
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Biophysics - Membrane Phenomena *10508
 Enzymes - Physiological Studies *10808
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 BC Hominidae *86215
 IT Major Concepts
 Behavior; Biochemistry and Molecular Biophysics; Cell Biology;
 Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell
 Biology); Neurology (Human Medicine, Medical Sciences); Psychiatry
 (Human Medicine, Medical Sciences)
 IT Chemicals & Biochemicals
 PROTEIN KINASE A; ISOPROTERENOL
 IT Miscellaneous Descriptors
 ACTIVITY; BETA-ADRENERGIC TRANSDUCTION CASCADE; BETA-ADRENOCEPTOR;
 BETA-ADRENOCEPTOR-CYCLIC AMP-PROTEIN KINASE A; FIBROBLAST;
 ISOPROTERENOL; MAJOR **DEPRESSION**; NEUROLOGY; PATIENT
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae)
 ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
 RN 142008-29-5 (PROTEIN KINASE A)
 7683-59-2 (ISOPROTERENOL)

 L114 ANSWER 18 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1996:467852 BIOSIS
 DN PREV199699190208
 TI Lack of effect of chronic **antidepressant** treatment on **G_s**
 and **G_i alpha**-subunit protein and mRNA levels in the rat cerebral
 cortex.
 AU Emamghoreishi, Masoumeh; Warsh, Jerry J.; Sibony, David; Li, Peter P. (1)
 CS (1) Sect. Biochem. Psychiatry, Clarke Inst. Psychiatry, 250 College St.,
 Toronto, ON M5T 1R8 Canada
 SO Neuropsychopharmacology, (1996) Vol. 15, No. 3, pp. 281-287.
 ISSN: 0893-133X.
 DT Article
 LA English
 AB Experimental evidence indicates that chronic **antidepressant**
 treatment in rats modifies the central nervous system beta-adrenoceptor
 signaling pathway at multiple sites including receptor, **G-**
 protein, adenylyl cyclase, and protein
 kinase A. In the present study, we examined the postreceptor effect of
 antidepressant treatment on the **protein** and mRNA levels
 of **stimulatory** and inhibitory **G protein**
 alpha-subunits (**G-alpha-s** and **G-**
 alpha-i) and beta-subunits in rats infused continuously with
 various **antidepressants** for 21 days. Chronic treatment with
 tricyclic (desipramine and amitriptyline) and monoamine oxidase inhibiting
 (tranylcypromine) **antidepressants** did not significantly affect
 the immunoreactivity levels of **G-alpha-s** (both 45- and
 52-kDa species), **G-alpha-il**, **Ga-i2**, **G**
 -beta-36, and **beta-35** in rat cerebral cortex. Similarly, the levels of
 mRNA encoding these **G protein** subunits remained
 unchanged subsequent to these drug treatments. In contrast, cortical
 beta-adrenoceptor number was significantly decreased by these treatments.
 These results suggest that the adaptive changes of rat cerebral cortical
 beta-adrenoceptor-**adenylyl cyclase** system often seen
 after chronic **antidepressant** treatment are not accompanied by
 changes in the abundance and gene expression of **G-alpha**
 -s, G-alpha-i, or G-beta proteins.
 CC Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Membrane Phenomena *10508
 Enzymes - Physiological Studies *10808
 Endocrine System - Neuroendocrinology *17020
 Nervous System - Physiology and Biochemistry *20504
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
 BC Muridae *86375
 IT Major Concepts
 Cell Biology; Endocrine System (Chemical Coordination and Homeostasis);
 Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell
 Biology); Nervous System (Neural Coordination); Pharmacology
 IT Chemicals & Biochemicals
ADENYL CYCLASE; PROTEIN KINASE A; DESIPRAMINE;
 AMITRIPTYLINE; TRANYLCYPROMINE; MONOAMINE OXIDASE
 IT Miscellaneous Descriptors
ADENYL CYCLASE; AMITRIPTYLINE;
ANTIDEPRESSANT-DRUG; BETA-ADRENOCEPTOR; CEREBRAL CORTEX;
 CHRONIC **ANTIDEPRESSANT** TREATMENT; DESIPRAMINE; ENZYME
 INHIBITOR-DRUG; **G-PROTEIN**; **GI ALPHA**
 -SUBUNIT **PROTEIN**; **GS ALPHA**-SUBUNIT
PROTEIN; MESSENGER RNA; MONOAMINE OXIDASE; MRNA; NERVOUS
 SYSTEM; PHARMACOLOGY; **PROTEIN KINASE A**; SIGNAL TRANSDUCTION;
 THERAPEUTIC METHOD; TRANYLCYPROMINE
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rat (Muridae)
 ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates
 RN 9012-42-4 (**ADENYL CYCLASE**)
 142008-29-5 (PROTEIN KINASE A)
 50-47-5 (DESIPRAMINE)
 50-48-6 (AMITRIPTYLINE)
 155-09-9 (TRANYLCYPROMINE)
 9001-66-5 (MONOAMINE OXIDASE)
 L114 ANSWER 19 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1996:427050 BIOSIS
 DN PREV199699158106
 TI Lack of effect of **antidepressants** on mononuclear leukocyte
G-protein levels or function in **depressed**
 outpatients.
 AU Young, L. Trevor (1); Li, Peter P.; Kamble, Arvind; Siu, Kin Po; Warsh,
 Jerry J.
 CS (1) Dep. Psychiatry, Fac. Health Sci., McMaster Univ., 1200 Main St. W.,
 Hamilton, ON L8N 3Z5 Canada
 SO Journal of Affective Disorders, (1996) Vol. 39, No. 3, pp. 201-207.
 ISSN: 0165-0327.
 DT Article
 LA English
 AB Evidence from studies in animal and cultured cell models suggests that
antidepressants (ADs) may enhance postreceptor signalling through
 the **G protein** coupled **adenyl**
cyclase (AC) pathways. To test whether this also occurs in
 patients receiving AD treatment, **G-protein**
 -activated-AC activity and the levels of **alpha-s** and
alpha-i were measured in mononuclear leukocytes (MNLs) from 12
 subjects with major **depressive** disorder (MDD) at baseline and
 after a 5 week trial of AD treatment. Although no differences were found
 in GTP-gamma-S- and forskolin-**stimulated** AC activity or the
 levels of **alpha-s** and **alpha-i** in MDD subjects compared
 with age- and sex-matched healthy subjects, pretreatment basal AC activity

was significantly lower in treatment responders compared with healthy subjects. No significant changes were evident in any of these biochemical measures following 5 weeks of AD treatment in the patient group as a whole or stratified by response. These findings do not support an effect of ADs on the **G-protein** AC pathway, at least in MNLs. Lower pretreatment basal AC activity in responders suggests some change(s) in post-receptor signalling processes may be associated with an increased likelihood of therapeutic response to ADs.

CC Behavioral Biology - Human Behavior 07004

Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

Pharmacology - Psychopharmacology *22026

BC Hominidae *86215

IT Major Concepts

Pharmacology; Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals

ADENYLYL CYCLASE; CYCLASE

IT Miscellaneous Descriptors

ADENYLYL CYCLASE; ANTIDEPRESSANT THERAPY;

BEHAVIORAL AND MENTAL DISORDERS; ENZYME SUBSTRATE; **G-**

PROTEIN; G-PROTEIN-ACTIVATED-

ADENYLYL CYCLASE PATHWAY; MAJOR DEPRESSIVE

DISORDER; MONONUCLEAR LEUKOCYTE; PATIENT; PHARMACOKINETICS;

PHARMACOLOGY; SECOND MESSENGER; THERAPEUTIC METHOD; THERAPEUTIC

RESPONSE

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

RN 9012-42-4 (**ADENYLYL CYCLASE**)

9074-90-2 (**CYCLASE**)

L114 ANSWER 20 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1996:233860 BIOSIS

DN PREV199698797989

TI Platelet phosphoinositide signaling system: An overstimulated pathway in **depression**.

AU Karege, Felicien (1); Bovier, Philippe; Rudolph, Waltraut; Gaillard, Jean-Michel

CS (1) Univ. Geneva Inst. Neuropsychiatry, 2 ch. Petit Bel-Air, CH-1225 Chene-Bourg, Geneva Switzerland

SO Biological Psychiatry, (1996) Vol. 39, No. 8, pp. 697-702.

ISSN: 0006-3223.

DT Article

LA English

AB In order to test a possible **depression**-associated defect in signal transduction, platelet **alpha2**-adrenergic-mediated phosphoinositide (PI) hydrolysis was measured, both in drug-free major **depressed** patients and in control healthy subjects. Results that express phospholipase C activity have shown significant increase in the metabolites of epinephrine-**stimulated** tritiated phosphatidyl-4,5-biphosphate (3H-PIP-2) with respect to basal activity (saline-stimulated). Thrombin (2 units) and 10 mM sodium fluoride (NaF) also induced an increase in 3H-PIP-2 metabolites. These increases were potentiated in drug-free **depressed** patients both in epinephrine- and thrombin-**stimulated** platelets. In contrast, sodium fluoride, which directly **stimulates G protein** without receptor interaction, did not differentiate between patients and controls with respect to PI hydrolysis. This result suggests a possible **depression**-associated defect in heterologous receptor-**G protein** interaction.

CC Cytology and Cytochemistry - Human 02508

Behavioral Biology - Human Behavior 07004

Biochemical Studies - General 10060

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Lipids 10066
 Biochemical Studies - Minerals 10069
 Enzymes - Physiological Studies *10808
 Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
 Endocrine System - Neuroendocrinology *17020
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 BC Hominidae *86215
 IT Major Concepts
 Blood and Lymphatics (Transport and Circulation); Endocrine System
 (Cheical Coordination and Homeostasis); Enzymology (Biochemistry and
 Molecular Biophysics); Neurology (Human Medicine, Medical Sciences);
 Psychiatry (Human Medicine, Medical Sciences)
 IT Chemicals & Biochemicals
 EPINEPHRINE; THROMBIN; SODIUM; PHOSPHOLIPASE C; **ADENYLATE**
 CYCLASE
 IT Miscellaneous Descriptors
 ADENYLATE CYCLASE; EPINEPHRINE;
 PHOSPHATIDYL-4,5-BIPHOSPHATE; PHOSPHOLIPASE C; SIGNAL TRANSDUCTION;
 SODIUM CHLORIDE; THROMBIN; 1,2-DIACYLGLYCEROL; 1,4,5-TRIPHOSPHATE
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae)
 ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
 RN 51-43-4 (EPINEPHRINE)
 9002-04-4 (THROMBIN)
 7440-23-5 (SODIUM)
 9001-86-9 (PHOSPHOLIPASE C)
 9012-42-4 (ADENYLATE CYCLASE)
 L114 ANSWER 21 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1995:554266 BIOSIS
 DN PREV199698568566
 TI Chronic **antidepressant** treatment facilitates **G**
 protein activation of **adenylyl cyclase** without
 altering **G protein** content.
 AU Chen, Jiang; **Rasenick, Mark M. (1)**
 CS (1) Dep. Physiol. Biophysics, Univ. Illinois Coll. Medicine, 901 S.
 Wolcott Ave., Chicago, IL 60612-7342 USA
 SO Journal of Pharmacology and Experimental Therapeutics, (1995) Vol. 275,
 No. 1, pp. 509-517.
 ISSN: 0022-3565.
 DT Article
 LA English
 AB It has been suggested that the molecular basis of **antidepressant**
 action involves postreceptor components. Results from our studies have
 suggested that a **G protein** (G-s) is one of
 those targets and that chronic **antidepressant** treatment
 facilitates the activation of **adenylyl cyclase** by
 G-salpa. This report represents an attempt to define
 which aspects of **G protein** function are altered by
 chronic **antidepressant** treatment. Rats were treated for 21 days
 with amitriptyline, desipramine, ABT 200 (a pyrrolidine with putative
 antidepressant effects) or electroconvulsive shock, and membranes
 were prepared from the cerebral cortexes. Each of these treatments caused
 an increase in membrane **adenylyl cyclase** assayed in
 the presence of guanyl-5'imidodiphosphate ($1 \mu\text{M}$). Results of
 acute **antidepressant** treatments were no different than those of
 control treatment. Chronic treatment with amphetamine, which inhibits
 neurotransmitter reuptake without displaying **antidepressant**
 effect, was also ineffective in increasing **G-salpa**
 stimulation of adenylyl cyclase. Chronic
 antidepressant treatment did not change the content of **G**
 protein, as no change at the level of **G-salpa**

, **G-ialpha**, **G-oalpha** or **G**
 -beta **protein** was detected by immunoblotting. Although there was
 no change in the amount of **G proteins**,
antidepressant treatment increased the number of active **G**
-salpha/adenylyl cyclase complexes
 immunoprecipitated by an anti-**G-salpha** antibody. It is
 suggested that chronic **antidepressant** treatment alters certain
 membrane components such that a greater proportion of **G-**
salpha is activated, **G-salpha** enjoys a more
 fruitful interaction with **adenylyl cyclase**, or both.

CC Biochemical Studies - General 10060
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Therapy *12512
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Nervous System - Physiology and Biochemistry *20504
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pharmacology - Clinical Pharmacology 22005
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Muridae *86375

IT Major Concepts
 Behavior; Biochemistry and Molecular Biophysics; Enzymology
 (Biochemistry and Molecular Biophysics); Metabolism; Nervous System
 (Neural Coordination); Pathology; Pharmacology

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE

IT Miscellaneous Descriptors
 ABT 200; AMITRIPTYLINE; **ANTIDEPRESSANT-DRUG**; DESIPRAMINE;
 MOLECULAR ACTIVITY; PHARMACODYNAMICS

ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 rat (Muridae)

ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
 50-48-6 (AMITRIPTYLINE)
 50-47-5 (DESIPRAMINE)

L114 ANSWER 22 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1995:516658 BIOSIS
 DN PREV199598530958
 TI Chronic **antidepressant** treatment increases coupling between the
G protein, Gs and **type VI**
adenylyl cyclase.

AU Chen, J.; Chaney, K.; **Rasenick, M. M.**
 CS Dep. Physiol. Biophysics, Univ. Ill. Coll. Med., Chicago, IL 60612 USA
 SO Society for Neuroscience Abstracts, (1995) Vol. 21, No. 1-3, pp. 1865.
 Meeting Info.: 25th Annual Meeting of the Society for Neuroscience San
 Diego, California, USA November 11-16, 1995
 ISSN: 0190-5295.

DT **Conference**
 LA English

CC **General Biology - Symposia, Transactions and Proceedings of**
Conferences, Congresses, Review Annuals 00520
 Cytology and Cytochemistry - Animal *02506
 Biochemical Studies - General 10060
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Membrane Phenomena *10508
 External Effects - Electric, Magnetic and Gravitational Phenomena 10610
 Enzymes - Physiological Studies *10808
 Nervous System - Physiology and Biochemistry *20504
 Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

BC Muridae *86375
 IT Major Concepts
 Cell Biology; Enzymology (Biochemistry and Molecular Biophysics);
 Membranes (Cell Biology); Nervous System (Neural Coordination);
 Pharmacology
 IT Chemicals & Biochemicals
 ADENYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE;
 AMPHETAMINE
 IT Miscellaneous Descriptors
 AMITRIPTYLINE; AMPHETAMINE; **ANTIDEPRESSANT-DRUG**; DESIPRAMINE;
 ELECTROCONVULSIVE SHOCK; MEETING ABSTRACT; MEETING POSTER; SIGNAL
 TRANSDUCTION
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rat (Muridae)
 ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates
 RN **9012-42-4 (ADENYL CYCLASE)**
 50-48-6 (AMITRIPTYLINE)
 50-47-5 (DESIPRAMINE)
 300-62-9 (AMPHETAMINE)

L114 ANSWER 23 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1995:515202 BIOSIS

DN PREV199598529502

TI Participation of vitamin B-12 in beta-receptor mediated regulation of
adenyl cyclase system.

AU Watanabe, M. (1); Hatta, S.; Ikeda, H. (1); **Toki, S. (1)**; Ozawa,
 H. (1); Saito, T. (1); Takahata, N. (1)

CS (1) Dep. Neuropsychiatry, Sch. Med., Sapporo Med. Univ., Sapporo 060 Japan

SO Society for Neuroscience Abstracts, (1995) Vol. 21, No. 1-3, pp. 1614.
 Meeting Info.: 25th Annual Meeting of the Society for Neuroscience San
 Diego, California, USA November 11-16, 1995
 ISSN: 0190-5295.

DT **Conference**

LA English

CC **General Biology - Symposia, Transactions and Proceedings of
 Conferences, Congresses, Review Annuals 00520**

Biochemical Studies - Vitamins 10063

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - Membrane Phenomena *10508

Enzymes - Physiological Studies *10808

Pathology, General and Miscellaneous - Therapy 12512

Metabolism - Water-Soluble Vitamins *13018

Nutrition - Malnutrition; Obesity *13203

Nutrition - Water-Soluble Vitamins *13210

Endocrine System - Neuroendocrinology *17020

Nervous System - Pathology *20506

Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

BC Hominidae 86215

Muridae *86375

IT Major Concepts

 Endocrine System (Chemical Coordination and Homeostasis); Enzymology
 (Biochemistry and Molecular Biophysics); Membranes (Cell Biology);
 Metabolism; Neurology (Human Medicine, Medical Sciences); Nutrition;
 Psychiatry (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals

 VITAMIN B12; **ADENYL CYCLASE**; MECOBALAMIN;
 S-ADENOSYL-L-METHIONINE

IT Miscellaneous Descriptors

 ALZHEIMER'S DISEASE; BETA-ADRENERGIC RECEPTOR; CLINICAL IMPLICATIONS;
 DEMENTIA; **DEPRESSION**; HUMAN MODEL; MECOBALAMIN; MEETING
 ABSTRACT; MEETING POSTER; S-ADENOSYL-L-METHIONINE; SCHIZOPHRENIA;

SIGNAL TRANSDUCTION CASCADE; VITAMIN B12 DEFICIENCY

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae:
Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

rat (Muridae); Hominidae (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; nonhuman mammals; nonhuman
vertebrates; primates; rodents; vertebrates

RN 68-19-9 (VITAMIN B12)

9012-42-4 (ADENYL CYCLASE)

13422-55-4 (MECOBALAMIN)

29908-03-0 (S-ADENOSYL-L-METHIONINE)

L114 ANSWER 24 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1995:161987 BIOSIS

DN PREV199598176287

TI Guanine nucleotide-binding proteins in bipolar affective disorder: Effects
of long-term lithium treatment.AU Manji, Hussein K. (1); Chen, Guang; Shimon, Hady; Hsiao, John K.; Potter,
William Z.; Belmaker, Robert H.CS (1) Sect. Clin. Pharmacol., NIMH, Build. 10, Room 2D46, 9000 Rockville
Pk., Bethesda, MD 20892 USASO Archives of General Psychiatry, (1995) Vol. 52, No. 2, pp. 135-144.
ISSN: 0003-990X.

DT Article

LA English

AB Background: This study examines recent suggestions from a number of investigators that signal-transducing guanine nucleotide-binding (G) proteins may be involved in the pathophysiology of bipolar affective disorder and may represent molecular targets for lithium's mood-stabilizing actions. Methods: We used selective antibodies to quantitate the levels of the G protein **alpha** subunits that regulate **adenylate cyclase** activity (G-**alpha**-s and G-**alpha**-i2) and phosphoinositide turnover (G-**alpha**-q/11). We also quantitated levels of pertussis toxin-catalyzed phosphate 32-labeled adenosine diphosphate ((32P)ADP) ribosylation in platelet and leukocyte membranes from a group of 14 untreated (predominantly manic) patients with bipolar affective disorder, 20 lithium-treated euthymic patients with bipolar affective disorder, and 11 healthy controls. Results: In both tissues, the immunolabeling of the 45-kd form of G-**alpha**-s was higher in the bipolar affective disorder group considered as a whole (treated or untreated) compared with controls, effects that reached statistical significance in the leukocyte membranes. There were no significant differences in the immunolabeling of G-**alpha**-i1/2, G-**alpha**-q/11, or pertussis toxin-catalyzed (32P)ADP ribosylation in either tissue in the untreated bipolar affective disorder group compared with controls. In both tissues, lithium-treated subjects demonstrated lower levels of G-**alpha**-q/11 and higher levels of pertussis toxin-catalyzed (32P)ADP-ribosylation, which reached significance in the platelet membranes. Conclusions: Our results are complementary to the previously reported findings of elevated G-**alpha**-s levels in postmortem brain tissue from patients with bipolar affective disorder and in mononuclear leukocytes obtained from depressed patients with bipolar (but not unipolar) affective disorder. The significantly higher levels of pertussis toxin-catalyzed (32P)ADP ribosylation in the subjects receiving long-term lithium-treatment replicates our findings in rat cortex and in healthy volunteers and adds to the growing body of evidence implicating G-**alpha**-i as a target of lithium's actions.

CC Cytology and Cytochemistry - Human *02508

Behavioral Biology - Human Behavior *07004

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Lipids 10066

Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Therapy *12512
 Metabolism - Lipids *13006
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
 Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and
 Reticuloendothelial System *15008
 Nervous System - Physiology and Biochemistry *20504
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pharmacology - Clinical Pharmacology *22005
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Hominidae *86215

IT Major Concepts

Behavior; Blood and Lymphatics (Transport and Circulation); Cell
 Biology; Enzymology (Biochemistry and Molecular Biophysics);
 Metabolism; Nervous System (Neural Coordination); Neurology (Human
 Medicine, Medical Sciences); Pathology; Pharmacology; Psychiatry (Human
 Medicine, Medical Sciences)

IT Chemicals & Biochemicals

LITHIUM; **ADENYLATE CYCLASE**

IT Miscellaneous Descriptors

ADENYLATE CYCLASE; ANTIPSYCHOTIC-DRUG; **G**
PROTEIN ALPHA-SUBUNIT; LITHIUM; MONONUCLEAR
 LEUKOCYTE; MOOD-STABILIZING ACTION; PATHOPHYSIOLOGY; PHARMACODYNAMICS;
 PHOSPHOINOSITIDE TURNOVER

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

RN 7439-93-2 (LITHIUM)

9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 25 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1995:131482 BIOSIS

DN PREV199598145782

TI Chronic treatment of C6 glioma cells with **antidepressant** drugs
 increases functional coupling between a **G protein** (
G-s) and **adenylyl cyclase**.

AU Chen, Jiang; **Rasenick, Mark M.** (1)

CS (1) Dep. Physiol. Biophysics, Univ. Illinois Coll. Med., 901 S. Wolcott
 Ave., m/c 901, Chicago, IL 60612-7342 USA

SO Journal of Neurochemistry, (1995) Vol. 64, No. 2, pp. 724-732.
 ISSN: 0022-3042.

DT Article

LA English

AB It has been reported that **antidepressant** treatment in rats
 results in a significant increase of **G-s**-mediated
stimulation of adenylyl cyclase and this
 effect correlates well with the clinical therapeutic response. This
 increased activity occurs despite a down-regulation of several receptors
 linked normally to the **stimulation** of that enzyme. To
 distinguish between these effects and to determine whether presynaptic
 components of the cell are required, C6 glioma cells were treated with
antidepressants. Tricyclic (amitriptyline and desipramine) or
 atypical (iprindole) **antidepressant** exposure to C6 cells for 5
 days significantly increased guanylyl-5'-imidodiphosphate (Gpp(NH)p)-
stimulated adenylyl cyclase activity in
 membrane preparations in a manner similar to that seen for rat brain
 membranes after 21-day treatment. This effect was drug dose and exposure
 time dependent. Nevertheless, **stimulation of adenylyl**
cyclase by isoproterenol was decreased after

antidepressant treatment. By comparison, the **antidepressant**-induced beta-receptor desensitization occurred earlier than the enhancement of Gpp(NH)p-activated **adenylyl cyclase**, and extensive desensitization of beta receptors by isoproterenol treatment did not enhance the Gpp(NH)p-stimulated **adenylyl cyclase** activity. These results indicated that the **antidepressant** has a direct effect on cell signaling and this enhanced Gpp(NH)p-stimulated **adenylyl cyclase** activity is not correlated with desensitization of beta-adrenergic receptor stimulated **adenylyl cyclase**. These data contribute to the suggestion that **G proteins** (especially **G-s**) are the target of **antidepressant** actions. Immunoblotting showed that neither the number of **G protein** subunits (**alpha-s**, **alpha-i**, **alpha-o**, and **beta**) nor their association with the plasma membrane was changed after **antidepressant** treatment. Thus, these results are consistent with the hypothesis that chronic **antidepressant** treatment acts directly at the postsynaptic membrane to increase the coupling between **G-s** and **adenylyl cyclase**.

- CC Cytology and Cytochemistry - Animal *02506
 Behavioral Biology - Animal Behavior *07003
 Behavioral Biology - Human Behavior *07004
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Biophysics - Membrane Phenomena *10508
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Therapy *12512
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Endocrine System - Neuroendocrinology *17020
 Nervous System - Physiology and Biochemistry *20504
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pharmacology - Endocrine System *22016
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
 Neoplasms and Neoplastic Agents - Biochemistry *24006
- BC Hominidae 86215
 Muridae *86375
- IT Major Concepts
 Behavior; Biochemistry and Molecular Biophysics; Cell Biology;
 Endocrine System (Chemical Coordination and Homeostasis); Enzymology
 (Biochemistry and Molecular Biophysics); Membranes (Cell Biology);
 Metabolism; Nervous System (Neural Coordination); Neurology (Human
 Medicine, Medical Sciences); Oncology (Human Medicine, Medical
 Sciences); Pathology; Pharmacology; Psychiatry (Human Medicine, Medical
 Sciences)
- IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE;
IPRINDOLE
- IT Miscellaneous Descriptors
AMITRIPTYLINE; ANTIDEPRESSANT-DRUG; BETA-ADRENERGIC RECEPTOR;
BRAIN; DEPRESSION; DESIPRAMINE; G-S PROTEIN
; GTP BINDING PROTEIN; IPRINDOLE; PHARMACODYNAMICS;
POSTSYNAPTIC MEMBRANE; RECEPTOR-EFFECTOR COUPLING; TRICYCLIC
ANTIDEPRESSANT AGENT
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae:
 Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 rat (Muridae); Hominidae (Hominidae)
- ORGN Organism Superterms
 animals; chordates; humans; mammals; nonhuman mammals; nonhuman
 vertebrates; primates; rodents; vertebrates

RN 9012-42-4 (ADENYLYL CYCLASE)
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 26 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:50814 BIOSIS
DN PREV199598065114
TI Augmented **adenylyl cyclase** activation by chronic
antidepressant treatment of C6 glioma cells is due to facilitated
G protein coupling.
AU Chen, J.; **Rasenick, M. M.**
CS Dep. Physiol. Biophysics, Univ. Illinois Coll. Med., Chicago, IL
60612-7342 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 21A.
Meeting Info.: Thirty-fourth Annual Meeting of the American Society for
Cell Biology San Francisco, California, USA December 10-14, 1994
ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**
Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules 10506
Biophysics - Membrane Phenomena *10508
Enzymes - Chemical and Physical *10806
Nervous System - Physiology and Biochemistry *20504
BC Muridae *86375
IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics);
Membranes (Cell Biology); Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE;
IPRINDOLE
IT Miscellaneous Descriptors
AMITRIPTYLINE; BETA ADRENERGIC RECEPTOR; DESIPRAMINE; IPRINDOLE;
MEETING ABSTRACT; MEETING POSTER
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rat (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
rodents; vertebrates

RN 9012-42-4 (ADENYLYL CYCLASE)
50-48-6 (AMITRIPTYLINE)
50-47-5 (DESIPRAMINE)
5560-72-5 (IPRINDOLE)

L114 ANSWER 27 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:472567 BIOSIS
DN PREV199497485567
TI Functional activation of C6 glioma **adenylyl cyclase** by
G-protein after chronic exposure to
antidepressant is independent of receptor desensitization.
AU Chen, J.; **Rasenick, M. M.**
CS Dep. Physiol. Biophys., Univ. Illinois Coll. Med., Chicago, IL 60612-7342
USA
SO Society for Neuroscience Abstracts, (1994) Vol. 20, No. 1-2, pp. 436.
Meeting Info.: 24th Annual Meeting of the Society for Neuroscience Miami
Beach, Florida, USA November 13-18, 1994
ISSN: 0190-5295.
DT **Conference**
LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
 Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Membrane Phenomena *10508
 Enzymes - Physiological Studies *10808
 Nervous System - Pathology *20506
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Muridae *86375

IT Major Concepts
 Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Nervous System (Neural Coordination); Pharmacology

IT Chemicals & Biochemicals
ADENYLYL CYCLASE; AMITRIPTYLINE; DESIPRAMINE;
 IPRINDOLE

IT Miscellaneous Descriptors
 AMITRIPTYLINE; **ANTIDEPRESSANT-DRUG**; DESIPRAMINE; IPRINDOLE;
 MEETING ABSTRACT; MEETING SLIDE

ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 rat (Muridae)

ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates

RN **9012-42-4 (ADENYLYL CYCLASE)**
 50-48-6 (AMITRIPTYLINE)
 50-47-5 (DESIPRAMINE)
 5560-72-5 (IPRINDOLE)

L114 ANSWER 28 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1994:117447 BIOSIS

DN PREV199497130447

TI **Adenylyl cyclase** activity and G-
protein subunit levels in postmortem frontal cortex of suicide
 victims.

AU Cowburn, Richard F. (1); Marcusson, Jan O.; Eriksson, Anders; Wiehager,
 Birgitta; O'Neill, Cora

CS (1) Dep. Geriatric Med. B56, Karolinska Inst., Huddinge Univ. Hosp., S-141
 86 Huddinge Sweden

SO Brain Research, (1994) Vol. 633, No. 1-2, pp. 297-304.
 ISSN: 0006-8993.

DT Article

LA English

AB Basal and **stimulated adenylyl cyclase**
 activities and G-s and G-i **protein** a-subunit
 levels (**G-salpa** and **G-ialpha**)
 were compared in postmortem frontal cortex from 18 suicide cases and 22
 matched controls. Basal, guanosine 5'-O-(3-thiotriphosphate) (GTP-gamma-S)
stimulated and forskolin **stimulated** enzyme activities
 were significantly lower in the suicide cases, compared to controls. These
 effects were most apparent in those suicides that had died from violent
 means or that had had a history of **depression** and appeared to
 reflect the lowered basal activity rather than a reduced ability of either
 GTP-gamma-S or forskolin to activate the enzyme. No significant
 correlations were found between **adenylyl cyclase**
 activity and either subject age or postmortem delay. Western blotting
 revealed no significant differences in **G-salpa** and
G-ialpha levels between control and suicide cases.
 However, levels of the smaller **G-salpa** isoform (
G-salpa-S) showed a tendency to be increased in the
 violent death suicide and **depressed** suicide subgroups, compared
 to controls. Levels of the larger **G-salpa** isoform (
G-salpa-L) showed a significant positive correlation

with subject age. **G-ialpha.** levels showed a significant negative correlation with subject age and a positive correlation with postmortem delay. These results support the hypothesis that suicidal behaviour and **depressive** illness may be associated with an altered regulation of **adenylyl cyclase**.

- CC Behavioral Biology - Human Behavior *07004
 Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biochemical Studies - Lipids 10066
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Necrosis *12510
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
 Pharmacology - Drug Metabolism; Metabolic Stimulators 22003
 Pharmacology - Neuropharmacology *22024
- BC Hominidae *86215
- IT Major Concepts
 Behavior; Enzymology (Biochemistry and Molecular Biophysics);
 Metabolism; Neurology (Human Medicine, Medical Sciences); Pathology;
 Psychiatry (Human Medicine, Medical Sciences)
- IT Chemicals & Biochemicals
ADENYLYL CYCLASE
- IT Miscellaneous Descriptors
DEPRESSION
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 human (Hominidae)
- ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
- RN **9012-42-4 (ADENYLYL CYCLASE)**
- L114 ANSWER 29 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
- AN 1994:50907 BIOSIS
- DN PREV199497063907
- TI Effect of chronic **antidepressant** treatment on tubulin function
 in rat brain.
- AU Kamada, H. (1); Saito, T. (1); Ozawa, H. (1); Hatta, S.; Hashimoto, E.
 (1); Ashizawa, T. (1); **Rasenick, M. M.**; Takahata, N. (1)
- CS (1) Dep. Neuropsychiatry, Sapporo Med. Univ., Sapporo 060 Japan
- SO Society for Neuroscience Abstracts, (1993) Vol. 19, No. 1-3, pp. 939.
 Meeting Info.: 23rd Annual Meeting of the Society for Neuroscience
 Washington, D.C., USA November 7-12, 1993
 ISSN: 0190-5295.
- DT **Conference**
- LA English
- CC **General Biology - Symposia, Transactions and Proceedings of
 Conferences, Congresses, Review Annuals 00520**
 Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Enzymes - Physiological Studies *10808
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Nervous System - Pathology *20506
 Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
 Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
 Toxicology - Pharmacological Toxicology *22504
- BC Muridae *86375
- IT Major Concepts
 Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Nervous
 System (Neural Coordination); Pharmacology; Toxicology
- IT Chemicals & Biochemicals

AMITRIPTYLINE; ADENYLATE CYCLASE

IT Miscellaneous Descriptors

**ADENYLATE CYCLASE; AMITRIPTYLINE; MEETING ABSTRACT;
MEETING POSTER; TOXICITY**

ORGN Super Taxa

Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

Muridae (Muridae)

ORGN Organism Superterms

animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals;
rodents; vertebrates

RN 50-48-6 (AMITRIPTYLINE)

9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 30 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1994:4483 BIOSIS

DN PREV199497017483

TI Chronic **antidepressant** treatment changes **G
protein** functional interactions without altering **G
protein** content.AU Chen, J.; **Rasenick, M. M.**

CS Dep. Physiol. and Biophys., Univ. Ill. Chicago, Chicago, IL 60612-7384 USA

SO Society for Neuroscience Abstracts, (1993) Vol. 19, No. 1-3, pp. 309.

Meeting Info.: 23rd Annual Meeting of the Society for Neuroscience

Washington, D.C., USA November 7-12, 1993

ISSN: 0190-5295.

DT **Conference**

LA English

CC **General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520**

Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General 10060

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - Membrane Phenomena *10508

Enzymes - Physiological Studies *10808

Pathology, General and Miscellaneous - Therapy *12512

Nervous System - Pathology *20506

Psychiatry - Psychopathology; Psychodynamics and Therapy 21002

Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

BC Muridae *86375

IT Major Concepts

Cell Biology; Enzymology (Biochemistry and Molecular Biophysics);

Membranes (Cell Biology); Nervous System (Neural Coordination);

Pathology; Pharmacology

IT Chemicals & Biochemicals

ADENYLYL CYCLASE

IT Miscellaneous Descriptors

ADENYLYL CYCLASE; CEREBRAL CORTEX; MEETING**ABSTRACT; MEETING POSTER; PLASMA MEMBRANE**

ORGN Super Taxa

Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

rat (Muridae)

ORGN Organism Superterms

animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
rodents; vertebratesRN **9012-42-4 (ADENYLYL CYCLASE)**

L114 ANSWER 31 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1992:534656 BIOSIS

DN BR43:120356

TI EFFECTS OF **ANTIDEPRESSANTS** AND ELECTROCONVULSIVE SHOCK ON
COUPLING OF **G PROTEIN** TO **ADENYLATE
CYCLASE**.

AU OZAWA H; HATTA S; RASENICK M M; TAKAHATA N; SAITO T
 CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO 060, JAPAN.
 SO RACAGNI, G., N. BRUNELLO AND T. FUKUDA (ED.). INTERNATIONAL CONGRESS
 SERIES, NO. 968. BIOLOGICAL PSYCHIATRY, VOLS. 1 AND 2; PROCEEDINGS OF THE
 5TH WORLD CONGRESS OF BIOLOGICAL PSYCHIATRY, FLORENCE, ITALY, JUNE 9-14,
 1991. XXVIII+886P.(VOL. 1); XXXI+949P.(VOL. 2) ELSEVIER SCIENCE PUBLISHERS
 B.V.: AMSTERDAM, NETHERLANDS; (DIST. IN THE USA AND CANADA BY ELSEVIER
 SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK, USA). ILLUS. (1991) 0
 (0), 188-191.
 CODEN: EXMDA4. ISSN: 0531-5131. ISBN: 0-444-81410-8 (VOL. 1),
 0-444-89295-8 (VOL. 2), 0-444-89296-6 (SET).

DT **Conference**

FS BR; OLD

LA English

CC **General Biology - Symposia, Transactions and Proceedings of
 Conferences, Congresses, Review Annuals 00520**

Behavioral Biology - Animal Behavior *07003

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

External Effects - Electric, Magnetic and Gravitational Phenomena *10610

Enzymes - Physiological Studies *10808

Pathology, General and Miscellaneous - Therapy 12512

Metabolism - Proteins, Peptides and Amino Acids *13012

Metabolism - Nucleic Acids, Purines and Pyrimidines *13014

Nervous System - Pathology *20506

Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

Laboratory Animals - General 28002

BC Muridae 86375

IT Miscellaneous Descriptors

RAT MODEL PHARMACOKINETICS PHARMACODYNAMICS GTP ADP

RN 86-01-1 (GTP)

9012-42-4 (ADENYLATE CYCLASE)

58-64-0Q, 7722-76-1Q (ADP)

L114 ANSWER 32 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1990:460106 BIOSIS

DN BR39:95467

TI ACCELERATED GUANINE NUCLEOTIDE EXCHANGE BETWEEN GI AND GS AND
 ENHANCED COUPLING OF GS TO ADENYLATE CYCLASE
 SUBSEQUENT TO CHRONIC ANTIDEPRESSANT TREATMENT.

AU OZAWA H; SAITO T; RASENICK M M; TAKAHATA N

CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO 060, JPN.

SO NISHIZUKA, Y., M. ENDO AND C. TANAKA (ED.). ADVANCES IN SECOND MESSENGER
 AND PHOSPHOPROTEIN RESEARCH, VOL. 24. THE BIOLOGY AND MEDICINE OF SIGNAL
 TRANSDUCTION; 7TH INTERNATIONAL CONFERENCE ON CYCLIC NUCLEOTIDES, CALCIUM
 AND PROTEIN PHOSPHORYLATION, KOBE, JAPAN, OCTOBER 8-13, 1989. XXXIII+750P.
 RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. (1990) 0 (0), 562.

CODEN: ASMRE5. ISBN: 0-88167-670-5.

DT **Conference**

FS BR; OLD

LA English

CC **General Biology - Symposia, Transactions and Proceedings of
 Conferences, Congresses, Review Annuals 00520**

Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General 10060

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Enzymes - Physiological Studies *10808

Nervous System - Pathology *20506

Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

Toxicology - Pharmacological Toxicology *22504

BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT RAT CEREBRAL SYNAPSES DRUG TOXICITY SIGNAL TRANSDUCTION
RN 9012-42-4 (ADENYLATE CYCLASE)
73-40-5Q, 69257-39-2Q (GUANINE)

L114 ANSWER 33 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:393028 BIOSIS
DN BR39:63989
TI INCREASED COUPLING OF **STIMULATORY G PROTEIN**
TO **ADENYLATE CYCLASE** SUBSEQUENT TO CHRONIC
ADMINISTRATION OF **ANTIDEPRESSANTS**.
AU OZAWA H; **RASENICK M M**; SAITO T; TAKAHATA N
CS DEP. NEUROPSYCHIATRY, SAPPORO MED. COLL., SAPPORO, JPN.
SO 5TH WORKSHOP FOR THE BIOCHEMICAL AND PHARMACOLOGICAL RESEARCH ON AFFECTIVE
DISORDERS, TOKYO, JAPAN, MAY 26-27, 1989. JPN J PSYCHIATRY NEUROL. (1990)
44 (1), 131-132.
CODEN: JJPNEA. ISSN: 0912-2036.

DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**
Conferences, Congresses, Review Annuals 00520
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026

BC Muridae 86375
IT Miscellaneous Descriptors
RAT DESIPRAMINE AMITRIPTYLINE IPRINDOLE **ANTIDEPRESSANT AGENT**
GTP-BINDING PROTEIN ANIMAL MODEL
RN 50-47-5 (DESIPRAMINE)
50-48-6 (AMITRIPTYLINE)
5560-72-5 (IPRINDOLE)
9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 34 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1990:120935 BIOSIS
DN BR38:55145
TI CHRONIC **ANTIDEPRESSANT** TREATMENT AUGMENTS COUPLING OF THE GTP
BINDING PROTEIN **GS** TO THE CATALYTIC MOIETY OF **ADENYLATE**
CYCLASE.
AU OZAWA H; **RASENICK M M**
CS PHYSIOL. AND BIOPHYS., UNIV. ILL. COLL. MED., CHICAGO, ILL. 60680.
SO 19TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PHOENIX, ARIZONA,
USA, OCTOBER 29-NOVEMBER 3, 1989. SOC NEUROSCI ABST. (1989) 15 (1), 853.
CODEN: ASNEE5.

DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**
Conferences, Congresses, Review Annuals 00520
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Energy and Respiratory Metabolism *13003
Metabolism - Proteins, Peptides and Amino Acids *13012
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
Laboratory Animals - General 28002

BC Muridae 86375
IT Miscellaneous Descriptors

ABSTRACT RAT

RN 9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 35 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1990:73865 BIOSIS

DN BA89:41691

TI COUPLING OF THE **STIMULATORY GTP-BINDING PROTEIN****G-S TO RAT SYNAPTIC MEMBRANE ADENYLATE CYCLASE**IS ENHANCED SUBSEQUENT TO CHRONIC **ANTIDEPRESSANT** TREATMENT.AU OZAWA H; **RASENICK M M**CS DEP. PHYSIOL. BIOPHYS., UNIV. ILL. CHICAGO COLL. MED., P.O. BOX 6998,
CHICAGO, ILL. 60680.

SO MOL PHARMACOL, (1989) 36 (5), 803-808.

CODEN: MOPMA3. ISSN: 0026-895X.

FS BA; OLD

LA English

AB In an attempt to resolve a unified postreceptor mechanism of action for **antidepressant** therapy, rats were treated with amitriptyline, desipramine or iprindole. Chronic treatment with these **antidepressant** drugs increased guanylylimidodiphosphate-[Gpp(NH)p-], NaF-, or forskolin-activated **adenylate cyclase** in synaptic membranes prepared from cerebral cortexes of treated rats. Gpp(NH)p-dependent inhibition of **adenylate cyclase** was unaffected. Maximal binding of the photoaffinity GTP analog azidoanilido-GTP (AAGTP) to the **adenylate cyclase stimulatory (Gs.alpha.)** and inhibitory (Gi.alpha.) **G proteins** was unaffected by **antidepressant** treatment. The chemical elimination of **Gs** (low pH treatment) eliminated all differences between control and **antidepressant**-treated groups. Further, nonneural tissues from rats receiving chronic **antidepressants** showed no changes in **adenylate cyclase** activity or AAGTP binding. The results of these studies suggest that chronic **antidepressant** administration promoted increased coupling between **Gs** and catalytic unit of **adenylate cyclase**. Thus, the molecular locus of **antidepressant** action may reside at the **stimulatory GTP-binding protein, Gs**.

CC Behavioral Biology - Animal Behavior *07003

Biochemical Studies - General 10060

Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - Molecular Properties and Macromolecules *10506

Biophysics - Membrane Phenomena *10508

Enzymes - Physiological Studies *10808

Metabolism - Proteins, Peptides and Amino Acids *13012

Nervous System - Physiology and Biochemistry *20504

Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

Pharmacology - Neuropharmacology *22024

Pharmacology - Psychopharmacology *22026

BC Muridae 86375

IT Miscellaneous Descriptors

AMITRIPTYLINE DESIPRAMINE IPRINDOLE **ANTIDEPRESSANT-DRUG**GUANYLYLIMIDODIPHOSPHATE **ADENYLATE CYCLASE**

RN 50-47-5 (DESIPRAMINE)

50-48-6 (AMITRIPTYLINE)

5560-72-5 (IPRINDOLE)

9012-42-4 (ADENYLATE CYCLASE)

L114 ANSWER 36 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1989:22065 BIOSIS

DN BR36:9742

TI ENHANCED COUPLING OF **G PROTEINS TO ADENYLATE****CYCLASE** SUBSEQUENT TO CHRONIC **ANTIDEPRESSANT** TREATMENT.AU OZAWA H; **RASENICK M M**

CS DEP. PHYSIOL. BIOPHYSICS, UNIV. ILL. COLL. OF MED., CHICAGO, ILL. 60680.

SO 18TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, TORONTO, ONTARIO,

CANADA, NOVEMBER 13-18, 1988. SOC NEUROSCI ABSTR. (1988) 14 (1), 576.
CODEN: ASNEE5.

DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids 13012
Nervous System - General; Methods 20501
Nervous System - Pathology *20506
Pharmacology - Neuropharmacology *22024
Pharmacology - Psychopharmacology *22026
BC Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT RAT AMITRIPTYLINE IMIPRAMINE IPRINDOL
RN 50-48-6 (AMITRIPTYLINE)
50-49-7 (IMIPRAMINE)
9012-42-4 (ADENYLATE CYCLASE)

=> fil medline

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FILE LAST UPDATED: 17 MAR 2002 (20020317/UP). FILE COVERS 1958 TO DATE.

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The OLDMEDLINE file segment now contains data from 1958 through 1965.
Enter HELP CONTENT for details.

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SUBSTANCE IDENTIFICATION.

=> d all tot 1158

L158 ANSWER 1 OF 4 MEDLINE
AN 2000110747 MEDLINE
DN 20110747 PubMed ID: 10646827
TI Platelet alpha2A-adrenoceptor function in major depression: Gi coupling, effects of imipramine and relationship to treatment outcome.
AU Gurguis G N; Vo S P; Griffith J M; Rush A J
CS Mental Health Services, Department of Veterans Affairs Medical Center, Dallas, TX, USA.. gurguis.george@dallas.va.gov
SO PSYCHIATRY RESEARCH, (1999 Dec 20) 89 (2) 73-95.
Journal code: QC4; 7911385. ISSN: 0165-1781.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000218
Last Updated on STN: 20000218

Entered Medline: 20000208

AB Studies suggest alpha2A-adrenoceptors (alpha(2A)AR) dysregulation in major depressive disorder (MDD). Platelet alpha(2A)ARs exist in high- and low-conformational states that are regulated by Gi protein. Although alpha(2A)AR coupling to Gi protein plays an important role in signal transduction and is modulated by antidepressants, it has not been previously investigated. Alpha2AR density in the high- and low-conformational states, agonist affinity and coupling efficiency were investigated in 27 healthy control subjects, 23 drug-free MDD patients and 16 patients after imipramine treatment using [3H]yohimbine saturation and norepinephrine displacement of [3H]yohimbine binding experiments. Coupling measures were derived from NE-displacement experiments. Patients had significantly higher alpha(2A)AR density, particularly in the high-conformational state, than control subjects. Coupling indices were normal in patients. High pre-treatment agonist affinity to the receptor in the high-conformational state and normal coupling predicted positive treatment outcome. Decreased coupling to Gi predicted a negative treatment outcome. Imipramine induced uncoupling (-11%) and redistribution of receptor density in treatment responders only, but had no effect on alpha(2A)AR coupling or density in treatment non-responders. Increased alpha(2A)AR density may represent a trait marker in MDD. The results provide indirect evidence for abnormal protein kinase A (PKA) and protein kinase C (PKC) in MDD which may be pursued in future investigations.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't

Adrenergic Uptake Inhibitors: PD, pharmacology

*Adrenergic Uptake Inhibitors: TU, therapeutic use

Adult

Antidepressive Agents, Tricyclic: PD, pharmacology

***Antidepressive Agents, Tricyclic: TU, therapeutic use**

Biological Markers: BL, blood

Blood Platelets: DE, drug effects

*Blood Platelets: ME, metabolism

Case-Control Studies

*Depression, Involutional: BL, blood

*Depression, Involutional: DT, drug therapy

Depression, Involutional: PX, psychology

***G-Protein, Inhibitory Gi: BL, blood**

Imipramine: PD, pharmacology

***Imipramine: TU, therapeutic use**

Middle Age

Norepinephrine: ME, metabolism

Protein Binding

Protein Kinases: ME, metabolism

Psychiatric Status Rating Scales

*Receptors, Adrenergic, alpha-2: BL, blood

Receptors, Adrenergic, alpha-2: DE, drug effects

Treatment Outcome

Yohimbine: ME, metabolism

RN 146-48-5 (Yohimbine); 50-49-7 (Imipramine); 51-41-2 (Norepinephrine)

CN 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents, Tricyclic); 0

(Biological Markers); 0 (Receptors, Adrenergic, alpha-2); EC 2.7.1.37

(Protein Kinases); EC 3.6.1.- (**G-Protein, Inhibitory**

Gi)

L158 ANSWER 2 OF 4 MEDLINE

AN 2000086845 MEDLINE

DN 20086845 PubMed ID: 10618463

TI Neutrophil beta(2)-adrenoceptor function in major depression: G(s) coupling, effects of imipramine and relationship to treatment outcome.

AU Gurguis G N; Vo S P; Griffith J M; Rush A J

CS The Department of Veterans Affairs Medical Center, Dallas, TX, USA..

gurguis.george@dallas.va.gov

SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1999 Dec 15) 386 (2-3) 135-44.

Journal code: EN6; 1254354. ISSN: 0014-2999.

CY Netherlands

DT (CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)

LA English
 FS Priority Journals
 EM 200002
 ED Entered STN: 20000314
 Last Updated on STN: 20000314
 Entered Medline: 20000229

AB Abnormal beta(2)-adrenoceptor density and beta(2)-adrenoceptor-mediated cyclic adenosine monophosphate (cAMP) responses were inconsistently reported in major depressive disorder. Tricyclic antidepressants downregulate beta-adrenoceptor density and decrease coupling to **G(s) protein**. Abnormal beta-adrenoceptor coupling may exist in major depressive disorder and may relate to treatment response. We investigated beta(2)-adrenoceptor coupling to **G(s) protein** in 25 controls, 23 major depressive disorder drug-free patients and 16 major depressive disorder patients after chronic imipramine treatment using agonist displacement experiments. Pretreatment beta(2)-adrenoceptor coupling and density were normal in patients as a whole. Chronic imipramine induced beta(2)-adrenoceptor uncoupling. This effect was observed in treatment responders who had increased beta(2)-adrenoceptor density in the high-conformational state and supercoupling prior to treatment. Beta(2)-adrenoceptor density decreased after imipramine treatment. Treatment non-responders had seemingly normal pretreatment beta(2)-adrenoceptor function, which was not changed by imipramine. Differences in beta(2)-adrenoceptor regulation in major depressive disorder may underlie treatment response. The results indirectly implicate abnormal agonist-mediated beta(2)-adrenoceptor gene expression, **protein** kinase A, and **protein** kinase C in major depressive disorder.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't
 Adrenergic Uptake Inhibitors: TU, therapeutic use
 Adult
 *Antidepressive Agents, Tricyclic: TU, therapeutic use
 *Depression, Involutional: DT, drug therapy
 Depression, Involutional: ME, metabolism
 *G-Protein, Stimulatory Gs: ME, metabolism
 *Imipramine: TU, therapeutic use
 Middle Age
 Neutrophils: ME, metabolism
 *Receptors, Adrenergic, beta-2: ME, metabolism
 Regression Analysis
 Severity of Illness Index
 Treatment Outcome

RN 50-49-7 (Imipramine)
 CN 0 (Adrenergic Uptake Inhibitors); 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, beta-2); EC 3.6.1.- (G-Protein, Stimulatory Gs)

L158 ANSWER 3 OF 4 MEDLINE
 AN 1999332548 MEDLINE
 DN 99332548 PubMed ID: 10404469
 TI Adrenergic receptor function in panic disorder. II. Neutrophil beta 2 receptors: **Gs protein** coupling, effects of imipramine treatment and relationship to treatment outcome.
 AU Gurguis G N; Blakeley J E; Antai-Otong D; Vo S P; Orsulak P J; Petty F; Rush A J
 CS Department of Veterans Affairs Medical Center, Laboratory of Clinical Neuroscience, Dallas, TX 75216, USA.. gurguis.george@dallas.va.gov
 SO JOURNAL OF PSYCHIATRIC RESEARCH, (1999 Jul-Aug) 33 (4) 309-22. Ref: 115
 Journal code: JTJ; 0376331. ISSN: 0022-3956.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English

FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991227

AB Panic attacks are associated with increased autonomic symptoms, suggesting increased beta 2-adrenergic receptor (beta 2AR) function in PD. Tricyclic antidepressants downregulate beta AR function. Previous studies on beta AR function in PD, however, are inconsistent. We recently found increased beta AR coupling and density in neutrophils of symptomatic drug-free PD patients. This study evaluated beta AR coupling to **Gs protein** in 28 controls, 25 drug-free PD patients and 8 PD imipramine-treated patients. PD patients had significantly higher coupling and receptor density, particularly in the high-conformational state. Differences were more pronounced in patients with less depressive symptomatology. Treatment with imipramine was associated with decreased beta AR coupling and density in the high-conformational state. Several beta AR binding parameters were related to severity of anxiety symptoms and treatment outcome. Antidepressants downregulate beta AR density and induce uncoupling from **Gs protein** in PD. Future studies may investigate beta AR coupling in relationship to treatment outcome and the role of beta AR kinase in PD.

CT Check Tags: Comparative Study; Human; Male; Support, U.S. Gov't, Non-P.H.S.
*Adrenergic beta-Antagonists: PD, pharmacology
Adult
*Antidepressive Agents, Tricyclic: PD, pharmacology
*Antidepressive Agents, Tricyclic: TU, therapeutic use
*Binding, Competitive: DE, drug effects
Cell Count: DE, drug effects
Down-Regulation (Physiology): DE, drug effects
*G-Protein, Stimulatory Gs: DE, drug effects
*Imipramine: PD, pharmacology
*Imipramine: TU, therapeutic use
Middle Age
*Neutrophils: DE, drug effects
Neutrophils: ME, metabolism
Panic Disorder: DI, diagnosis
*Panic Disorder: DT, drug therapy
Panic Disorder: PX, psychology
Prospective Studies
Psychiatric Status Rating Scales
*Receptors, Adrenergic, beta-2: DE, drug effects
Receptors, Adrenergic, beta-2: ME, metabolism
Severity of Illness Index
Treatment Outcome

RN 50-49-7 (Imipramine)
CN 0 (Adrenergic beta-Antagonists); 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, beta-2); EC 3.6.1.- (G-Protein, Stimulatory Gs)

L158 ANSWER 4 OF 4 MEDLINE
AN 1999103182 MEDLINE
DN 99103182 PubMed ID: 9885796
TI Adrenergic receptor function in panic disorder. I. Platelet alpha 2 receptors: Gi protein coupling, effects of imipramine, and relationship to treatment outcome.
AU Gurguis G N; Antai-Otong D; Vo S P; Blakeley J E; Orsulak P J; Petty F; Rush A J
CS Department of Veterans Affairs Medical Center, Dallas, Texas 75216, USA.
SO NEUROPSYCHOPHARMACOLOGY, (1999 Feb) 20 (2) 162-76.
Journal code: ADQ; 8904907. ISSN: 0893-133X.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
 EM 199903
 ED Entered STN: 19990413
 Last Updated on STN: 20000303
 Entered Medline: 19990329

AB Various studies suggest alpha 2-adrenergic receptor (alpha 2AR) dysregulation in panic disorder (PD). Platelet alpha 2-AR exist in high- and low-conformational states as a function of their coupling to Gi protein. alpha 2AR coupling is important in signal transduction and is modulated by antidepressants. alpha 2AR density in the high- and low-conformational states, agonist affinity, and coupling efficiency were investigated in 21 healthy controls, 21 drug-free PD patients, and eight imipramine-treated patients using norepinephrine displacement of 3H-yohimbine binding. Percentage of receptors in the high-conformational state (%RH) and the ratio of the agonist dissociation constant to the receptor in the low-/high-conformational state (KL/KH), calculated from displacement experiments, were used as coupling indices. Patients had high alpha 2AR density in both conformational states. %RH and KL/KH ratio were significantly different, particularly in patients with Hamilton scale for depression (HAMD) scores > or = 15. Imipramine treatment (29 weeks) had no effect on alpha 2AR density or coupling, despite improvement in anxiety ratings. High pretreatment alpha 2AR density and coupling predicted low severity of anxiety after treatment. Increased alpha 2AR density and abnormal coupling may represent an adaptive mechanism or trait marker in PD.

CT Check Tags: Human; Male; Support, U.S. Gov't, Non-P.H.S.
 Adult
 Agoraphobia: BL, blood
 Agoraphobia: DT, drug therapy
 Agoraphobia: PX, psychology
Antidepressive Agents, Tricyclic: AE, adverse effects
***Antidepressive Agents, Tricyclic: TU, therapeutic use**
 Blood Platelets: DE, drug effects
 *Blood Platelets: ME, metabolism
 Down-Regulation (Physiology): DE, drug effects
***G-Protein, Inhibitory Gi: BL, blood**
Imipramine: AE, adverse effects
***Imipramine: TU, therapeutic use**
 *Panic Disorder: BL, blood
 *Panic Disorder: DT, drug therapy
 Psychiatric Status Rating Scales
 Radioligand Assay
 *Receptors, Adrenergic, alpha-2: BL, blood
Treatment Outcome

RN 50-49-7 (Imipramine)
 CN 0 (Antidepressive Agents, Tricyclic); 0 (Receptors, Adrenergic, alpha-2);
 EC 3.6.1.- (G-Protein, Inhibitory Gi)

=>.d his

(FILE 'HOME' ENTERED AT 14:45:38 ON 18 MAR 2002)
 SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:45:49 ON 18 MAR 2002

L1 5901 S ADENYLYL(L)CYCLASE
 L2 26403 S ADENYLATE(L)CYCLASE

FILE 'REGISTRY' ENTERED AT 14:46:34 ON 18 MAR 2002

L3 1 S 9012-42-4
 E ADENYLYL CYCLASE/CN
 L4 1 S E10
 L5 745 S ADENYLATE (L) CYCLASE
 L6 768 S ADENYL (L) CYCLASE
 L7 45 S ADENYLYL (L) CYCLASE
 L8 766 S L6-L7 NOT L3,L4

FILE 'HCAPLUS' ENTERED AT 14:47:51 ON 18 MAR 2002

L9 18651 S L3
L10 3 S L4
L11 1724 S L8
L12 3247 S ADENYL(L)CYCLASE
L13 33314 S L1,L2,L9-L12
L14 99 S L13 (L) TYPE (L) VI
L15 2 S L14 AND ?DEPRESS?
E G PROTEIN/CT
E E10+ALL
L16 3058 S E3-E5
L17 18566 S E2
L18 3145 S L16,L17 (L) ALPHA
L19 2873 S GS (L) ALPHA
L20 2516 S L18,L19 AND L13
L21 1 S L18,L19 AND L15
L22 59 S L20 AND ?DEPRESS?
L23 93 S GSALPHA
L24 76 S L23 AND L13
L25 2 S L24 AND ?DEPRESS?
L26 2 S L21,L25
L27 356 S L16,L17 AND ?DEPRESS?
L28 147 S L13 AND L27
E RASENICK M/AU
L29 75 S E4-E6
E DONATI R/AU
L30 15 S E3,E8-E10
E TOKI S/AU
L31 23 S E3,E6
L32 42 S L16-L19,L23 AND L29-L31
L33 9 S L32 AND ?DEPRESS?
L34 35 S L32 AND L13,L14
L35 8 S L34 AND ?DEPRESS?
L36 10 S L15,L21,L26,L33,L35
L37 6138 S L13,L14 AND L16-L19
L38 76 S L13,L14 AND L23
L39 3126 S L13,L14 AND GS
L40 6487 S L37-L39
E DRUG SCREENING/CT
E E3+ALL
L41 26 S L40 AND E2,E1
L42 2 S L40 AND E5+NT
L43 37 S L36,L41-L42
L44 79 S L40 AND CYTOSKEL?
L45 405 S L40 AND PLASMA(L)MEMBRAN?
L46 1682 S L40 AND CELL(L)MEMBRAN?
L47 1805 S L44-L46
E DEPRESSION/CT
E E4+ALL
L48 4553 S E1,E2
E MENTAL DISORDER/CT
E E3+ALL
L49 32582 S E4+NT
L50 4 S L48,L49 AND L47
L51 2 S L50 AND GS?
L52 1 S L51 NOT MICRODIALYSIS
L53 38 S L43,L52
L54 12 S L53 AND ?DEPRESS?
L55 11 S L54 NOT DNA/TI
L56 2 S L55 AND REVIEW
L57 1 S L56 AND HEART
L58 10 S L55 NOT L57
L59 27 S L53 NOT L55
L60 10 S L58 AND (G OR GS) (L) PROTEIN
L61 8 S L58 AND STIMUL?

L62 6 S L58 AND ALPHA
 L63 10 S L60-L62 AND L1,L2,L9-L62
 E BIPOLAR DISORDER/
 E BIPOLAR DISORDER/CT
 E E3+ALL
 L64 784 S E1,E2
 E MANIA/CT
 E E3+ALL
 L65 386 S E1,E2
 E PSYCHOSIS/CT
 E E3+ALL
 L66 1299 S E1,E2
 E DEMENTIA/CT
 E E3+ALL
 L67 2729 S E1,E2
 L68 34 S L64-L67 AND L13,L14
 L69 31 S L68 AND L1,L2,L16-L19,L23
 L70 15 S L68 AND (G OR GS) (L) PROTEIN
 L71 8 S L68 AND GS?
 L72 32 S L70,L71,L69
 L73 28 S L72 NOT 3/SC
 SEL DN 10 11
 L74 2 S L73 AND E1-E2
 L75 12 S L63,L74 AND L1,L2,L9-L74
 L76 12 S L75 AND (?DEPRESS? OR BIOPOLAR(L)DISORDER OR MENTAL OR GS? OR
 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 15:26:06 ON 18 MAR 2002

L77 5 S E3-E7

FILE 'REGISTRY' ENTERED AT 15:26:42 ON 18 MAR 2002

FILE 'HCAPLUS' ENTERED AT 15:26:54 ON 18 MAR 2002

FILE 'BIOSIS' ENTERED AT 15:28:07 ON 18 MAR 2002

L78 164 S E3-E5
 E RASENICK M/AU
 E DONATI R/AU
 L79 42 S E3,E5,E7
 E TOKI S/AU
 L80 80 S E3,E6
 L81 37345 S L13,L14
 L82 403 S GSALPHA?
 L83 1345 S GS(L)ALPHA
 L84 19075 S G(L)PROTEIN(L)?ALPHA?
 L85 2014 S L81 AND L82-L84
 L86 92 S L78-L80 AND L81
 L87 60 S L78-L80 AND L82-L84
 L88 30 S L86 AND L87
 L89 71 S L86,L87 AND 00520/CC
 L90 70 S L86,L87 AND CONFERENCE/DT
 L91 50 S L86,L87 NOT L89,L90
 L92 25 S L91 NOT ARTICLE/DT
 L93 72 S L89,L90
 L94 7 S L93 AND L88
 L95 4 S L94 AND ?DEPRESS?
 L96 21 S L93 AND ?DEPRESS?
 L97 21 S L95,L96
 L98 13 S 22026/CC AND L97
 L99 761781 S 21?/CC
 L100 150775 S 22026/CC
 L101 335 S L99,L100 AND L82-L84
 L102 57 S L101 AND L81
 L103 18 S L102 AND ?DEPRESS?
 L104 4 S L103 AND 00520/CC
 L105 4 S L103 AND CONFERENCE/DT

L106 15 S L98,L104,L105
 L107 7 S L97 NOT L106
 L108 22 S L106,L107
 L109 53 S L102 NOT L108
 L110 14 S L109 AND ?DEPRESS?
 L111 36 S L108,L110
 L112 34 S L111 AND (G(L)PROTEIN OR GS? OR ALPHA OR STIMUL?)
 L113 2 S L111 NOT L112
 L114 36 S L111-L113 AND L78-L113

FILE 'BIOSIS' ENTERED AT 15:41:11 ON 18 MAR 2002

FILE 'WPIX' ENTERED AT 15:45:03 ON 18 MAR 2002

L115 314 S L1,L2,L12
 L116 4 S L115 (L) TYPE (L) VI
 L117 6 S ADENYLCYCLASE OR ADENYLYLCYCLASE OR ADENYLATECYCLASE
 L118 318 S L115,L116,L117
 L119 36926 S GSALPHA? OR GS(L)ALPHA OR (GS OR G) (L)PROTEIN
 L120 90 S L118 AND L119
 L121 8 S L120 AND ?DEPRESS?
 E RASENICK M/AU
 E DONATI R/AU
 L122 4 S E3,E4
 E TOKI S/AU
 L123 29 S E3
 L124 1 S L122,L123 AND L118,L119
 L125 2184 S G PROTEIN
 L126 9 S GS PROTEIN
 L127 42 S GSALPHA? OR GS(L)ALPHA
 L128 139 S L125 (L)ALPHA
 L129 40 S L125-L128 AND L118
 L130 111169 S (N102 OR P831)/M0,M1,M2,M3,M4,M5,M6
 L131 31 S L130 AND L129
 L132 2 S L131 AND ?DEPRESS?

FILE 'CONFSCI' ENTERED AT 15:55:03 ON 18 MAR 2002

L133 1252 S L118
 L134 22 S L133 AND L125-L128

FILE 'MEDLINE' ENTERED AT 15:56:19 ON 18 MAR 2002

L135 29378 S L118
 L136 0 S L3 OR L4
 L137 4742 S L135 AND L119
 E G PROTEIN/CT
 E E4+ALL
 E E2+ALL
 L138 1872 S E19+NT AND L119
 L139 6203 S L137,L138
 L140 136 S F3./CT AND L139
 E GTP-BINDING PROTEINS/CT
 E E3+ALL
 L141 61 S E14 AND L140
 L142 494 S E41
 L143 22 S L142 AND L140
 L144 10 S L143 AND ?DEPRESS?
 E DEPRESSIVE DISORDER/CT
 E E3+ALL
 L145 53454 S E3+NT
 L146 40 S L145 AND L139
 L147 1 S L146 AND SCREEN?
 L148 93 S L141,L143,L144,L146
 L149 53 S L148 AND ?ALPHA?
 E RASENICK M/AU
 L150 60 S E4,E5
 E DONATI R/AU
 L151 29 S E3,E5

E TOKI S/AU
L152 93 S E3
L153 44 S L150-L152 AND L135-L149
E ANTIDEPRESSIVE AGENTS/CT
L154 71720 S E3+NT
L155 59 S L154 AND L137,L139,L143
L156 4 S TREATMENT OUTCOME/CT AND L155
L157 4 S TREATMENT OUTCOME+NT/CT AND L155
L158 4 S L156,L157
L159 8 S L155 AND L153
L160 47 S L155 NOT L156-L159

FILE 'MEDLINE' ENTERED AT 16:11:13 ON 18 MAR 2002